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Instant Power Spectrum Analysis of Heart Rate Variability During Orthostatic Tilt Using a Time-/Frequency-Domain Method

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Abstract

Background Spectral analysis of heart rate (HR) variability (HRV) requires, as a rule, some level of stationarity and, as a result, is inadequate to quantify biological transients. A time-/frequency-domain method (TF) was developed to obtain an instant spectral power (SP) of HRV during tilt.

Methods and Results HR was recorded by Holter monitoring in volunteers and analyzed with a TF, the smoothed pseudo–Wigner-Ville transformation (SPWVT), with the table inclination randomly set or continuously increased while the table rotated in head-up position. (1) The SPWVT assesses, beat by beat, the instant center frequency (ICF) of the SP. ICF correlates better with instant HR than the ratio of low- (LF) to high-frequency (HF) oscillations. The transient effect of tilt is better characterized as a shift of SP toward lower frequencies than by changes in amplitudes. (2) The method evidences variations of HR from one second to another. During the passage to head-up position, the vagal withdrawal and the sympathetic activation occur nearly simultaneously, as indicated by the instant changes in both LF and HF amplitudes and ICF. (3) The averaged results of the SPWVT give results similar to those previously obtained with autoregressive algorithms.

Conclusions The SPWVT is a new tool to explore HR transitions such as periods before episodes of arrhythmias on a time scale of one beat and allows quantification of an instant frequency index (ICF)

that closely reflects the instantaneous relationship between sympathetic and vagal modulations.

Measurement of HRV is a noninvasive approach based on ECG monitoring that allows an indirect evaluation of cardiovascular autonomic control.[12345678] Time- and frequency-domain techniques can be used.[4] The former methods represent the most common procedure, and a simple index such as the SD has been used extensively for risk stratification in cardiovascular pathophysiology. The “peak-valley” measurements, another example, are based on the detection of averaged oscillations.[67] Conversely, the frequency-domain approach uses spectral techniques to analyze the RR interval series as a complex sum of waveforms, decomposing with FFT[8] or AR algorithms[35] the relative powers of contributing frequencies into individual sinusoidal components. Both methods require an observation window in the range of 2 to 3 minutes and therefore an assumption of relative stationarity during this period.

Instantaneous measurements of biological transients are, however, of extreme interest. Physiological conditions such as exercise, vasovagal syncope, or periods preceding episodes of arrhythmias cannot be thoroughly analyzed with traditional spectral techniques. This study aims to use the SPWVT to perform an instant time-/frequency-domain analysis of the instant changes of autonomic control occurring during passive head-up tilt test. The SPWVT provides a spectral profile for nearly every beat. It will be shown that with this technique it is possible to calculate, in addition to spectral components, an ICF of each of these components and of the entire spectral power. ICF represents a global index of the instantaneous relationship between sympathetic and vagal modulation.

Methods

Study Populations

Two groups of nonsmoking healthy volunteers of either sex were selected. Absence of any medication was controlled. Oral informed consent was obtained from all subjects, and the studies were approved by the corresponding institution’s review board. None of the subjects experienced syncope or presyncopal symptoms during the recordings. Subjects were not allowed to sleep. To minimize a subject’s emotional arousal, we did not collect blood samples. The subjects were studied in a quiet, dimly lit room at a comfortable temperature (22°C to 24°C) after they consumed a light lunch free of alcohol and caffeine-containing beverages. They were loosely strapped to an electrically driven tilt table that had a foot rest. Stationary segments devoid of arrhythmias (2000 to 3000 RR intervals) were selected.

Group 1 (Random Tilt)

The group 1 subjects were from L. Sacco Hospital in Milan, Italy. The time- and the frequency-domain indexes of the HRV of these subjects have previously been published by two of us (N.M. and A.M.) using an AR analysis.[3] The population included 14 volunteers (median age, 44 years). For each subject, the surface ECG (CM_5) was recorded at 3 PM with a conventional AC amplifier on an FM instrumentation tape (Racal). After an adaptation period, analog data acquisition was initiated for resting conditions during 15 minutes under spontaneous breathing; the table was then rotated to an upright position (head-up tilt) that was maintained for 10 minutes. The inclination of the table was randomly set at 15°, 30°, 45°, 60°, and 90°. After each step, the subjects were moved to a horizontal position for 10 minutes. For each subject, the mean respiratory rate was measured. The entire procedure took 105 minutes. Data were analyzed off-line after appropriate analog-to-digital conversion at a rate of 300 samples per second with a 12-bit converter (data translation). The software for data acquisition and spectral analysis have been described.[19] In brief, from the ECG signal, a derivative/threshold algorithm provided the continuous series of RR intervals (tachogram). Group 1 was used primarily to compare the results of the Wigner-Ville method with those of the classic AR algorithms.

Group 2 (Continuous Tilt)

The group 2 subjects were from Lariboisière Hospital in Paris, France. The population included 21 young volunteers (median age, 22 years). All subjects were studied at 10 AM under metronome breathing at a frequency of 0.25 Hz. After 20 minutes of continuous recording for resting conditions, the table was rotated to an upright position at 90°, and recording was maintained for 20 minutes. The ECG was monitored by means of a three-channel Holter recorder (DelMar Avionics). Analog data were digitized at a 128-Hz sampling rate (7.8125 ms) on a Marquette laser playback disk (Marquette Electronics). Automatic detection and classification were reviewed to detect misdetection and misclassification. Annotated RR interval lists were then transferred to a personal computer. Group 2 was used primarily to show the potency of the method as a tool to explore a transient.

Data Analysis

HRV was analyzed with a time- and frequency-domain method of analysis, the SPWVT,[10,11] which has already been used to analyze biological signals, including HRV and respiration oscillations, in humans[12,13,14,15,16] and mice.[17] To be understood, the SPWVT needs a reduction of cross-terms,[13,14,18] which is obtained by use of an analytical signal with no negative frequencies instead of the real signal. The procedure is based on the Hilbert transform.[10] High resolution is achieved by independent time and frequency smoothing.[11,12,13,14,19] The SPWVT provides a spectral profile for nearly every beat, each depending on the preceding and subsequent events (Fig 1). Details concerning this technique have been published previously.[12,13,14,15]

Practical implementation includes resampling of RR series at 2 Hz to avoid artifactual peaks[20] and high-pass filtering so that very-low-frequency oscillations (<0.04 Hz) were removed. A spectrum was obtained every 0.5 second, and each spectrum is an array of 128 power values corresponding to 128 frequency values equally spaced. All calculations were implemented with a signal analysis–oriented software (Lary-C software developed by INRIA under Sildex environment, TNI). The results for the spectral power were expressed in ms^2. The SPWVT allows quantification of the spectral power of the oscillations of heart rate. The LF and HF oscillations were arbitrarily separated by use of the mean respiratory frequency (in group 1, this was measured for every subject; in group 2, subjects were under metronome breathing, and the respiratory frequency was at 0.25 Hz). The two limits of HF were respiratory frequency ±0.05 Hz (in group 2, HF is therefore between 0.20 and 0.30 Hz). The lower limit (0.04 Hz) of LF was determined by the filtering process as explained above. We did not study the very-low-frequency oscillations (<0.04 Hz). ICF values were calculated in the same way as the peak power frequency by use of the first moment of instant spectrum.[21] The time- and frequency-domain analysis required a 3D (Fig 1) or color representation. LF and HF were also expressed in normalized units, relative to the sum (LF+HF), according to previous reports.[39]

Statistical Analysis

Index values are expressed as mean±SD. The differences between supine and head-up position were calculated by Student's *t* test. Correlation analyses were performed with the Spearman rank-order coefficient.

Results

Random Tilt (Group 1)

Random tilt has been used primarily to validate the SPWVT compared with AR analysis both in terms of averaged spectral power and ICF. The two major oscillatory components of the power density spectrum, HF and LF, are shown in Fig 1. Also illustrated in this figure is the extreme instability of the spectral power when plotted against time, whatever the time scale, especially in the LF oscillation area. Such a variability—the spectral power can vary twofold to fourfold within a second—was unexpected and was observed on every record, whatever the inclination of the table, and is obviously undetectable by FFT or AR analysis. The spectral power of each group of oscillations can be computed. As expected, the significance of the results was improved by the normalization procedure, as already reported.[3] The angles of inclination of the table correlate with a decrease in HF normalized units and an increase in LF normalized units. The LF/HF ratio is consequently markedly enhanced (from 18±13 in the resting position to 32±25 at 90°) and also correlates with the angles of inclination (Table 1). The results of the spectral analysis obtained with the SPWVT are comparable to those previously reported.[3] Nevertheless, the global variability, ie, either the sum (HF+LF) (823±430 ms^2 in resting position and 831±820 ms^2 at 90°, *P*=NS, n=14) or the variance (2122±1483 ms^2 in resting position and 2024±2022 ms^2 at 90°, *P*=NS, n=14) of the RR interval, is not modified by the tilt and does not correlate with the angles of inclination (Table 1).

Continuous Tilt (Group 2)

Instant Relationships

FFT can calculate only an averaged frequency; only SPWVT can provide true ICFs. The SPWVT allows measurement of the spectral power nearly every beat, and it is then possible to determine the frequency of the instant center spectral power, called the ICF, in Hz, as also proposed for other time-frequency distributions,[22] and the frequency of the ICF of LF (Fig 2). When spectral analysis is performed at the beginning and at the end of the test, the average ICF shifts from 0.15 to 0.10 Hz. The average ICF of LF also shifts from 0.10 to 0.08 Hz (Table 2, Fig 2), which indicates that the tendency to shift toward lower frequency is detectable even in the rather restricted LF area. The shift in ICF matches the changes in spectral power (Table 2) and, for each individual ICF or ICF of LF, correlates with the instant values of the LF/HF ratio (Fig 3). ICF is a frequency parameter and does not depend on any a priori assumption, like the limit between HF and LF. In a given individual, the correlation of the RR interval with the instant LF/HF ratio is usually weak and nonlinear (*r*=−49, *P*<.01, Fig 3), as opposed to the correlation with ICF (*r*=.79, *P*<.001, Fig 3). As a rule, for a given individual, the RR interval correlates better (15 of 21 members of group 2) with ICF ($.30<r<.75$) than with the LF/HF ratio ($.40<r<.85$).

Study on Tilt Transition

The SPWVT allows representation of the spectral and frequency parameters with a resolution of half a second. Fig 4 shows typical representation. At time 7 minutes, the fall in RR interval occurs, and simultaneously the vagal oscillation amplitudes are withdrawn and both amplitude and period of LF change. The most pronounced modification is a shift in ICF toward lower frequency (from 0.17 to 0.10 Hz). The fall of ICF of LF occurs on a smaller scale. The figure also illustrates (a and b) the fact that the variations of ICF can be seen to coincide with RR oscillations. The simultaneous withdrawal of HF and changes in LF amplitude and period were reproducible findings. There is an important degree of interindividual variability among the 21 volunteers of group 2 in terms of response to tilt: (1) the acceleration of heart rate occurs within 2 to 3 minutes in 18 of 21 subjects (Fig 4) but lasted longer (5 to 8 minutes) in 3 of 21 cases. (2) The fall in ICF was pronounced and clear-cut as in Fig 4 in only 15 of 21 of the cases; in 6 cases, the tilt-induced changes in ICF were hidden by a considerable amount of variability of this frequency parameter. (3) The most salient feature in terms of instability is the existence of irregular periodic oscillations of ICF in steady-state conditions, as illustrated in Fig 4 at time 3 to 6 minutes or 12 to 18 minutes, with a period and amplitude of 1 minute and 0.03 to 0.10 Hz, respectively.

Discussion

The main findings of this study were the following. (1) The averaged modifications of HRV during the tilt were the same when the SPWVT was used to calculate spectral energy as those previously published with the FFT or AR algorithm. (2) The instant spectral analysis shows considerable interbeat variations of the heart rate. (3) The ICF and ICF of LF correlate with both the instant heart rate and the LF/HF ratio and are indexes of the instantaneous changes of the sympathovagal balance. (4) The transition phase of tilt can be studied at the scale of one beat both in terms of spectral power and ICF. During tilt, changes in heart rate, LF, and HF occur simultaneously and are accompanied by a sharp fall in ICF. The SPWVT is then a new tool to explore transitions in heart rate and HRV in terms of frequency changes.

Time-Frequency Methods

Compared with other time-frequency methods, the SPWVT has a good frequency resolution and satisfies most of the margin conditions as a Cohen class member.[22] This is the only time-frequency method that has already been used for biological purposes, and it has indeed previously been applied to heart rate,[21213141623] respiratory oscillations,[12131424] or blood pressure.[121314] The Wigner-Ville transform needs a reduction of cross-terms, which has been achieved in the SPWVT. The method shows in 3D the evolution of the spectral power second per second (Figs 1 and 4). Other methods have been proposed, such as the method of Choi and Williams,[25] which is another smoothing of the Wigner-Ville transform. In this method, the smoothing is nonindependent in time and frequency and more efficient in two orthogonal directions of the time-frequency plane. Therefore, such a distribution is better selected when the components of the signal are not simultaneously detected.[11] A recent study compared the different methods available to track the transients during autonomic tests,[26] namely the method of Choi and Williams, implemented in a form called running windowed exponential distribution; the short-time Fourier transform; two AR methods (the modified covariance method and the fast recursive least-squares algorithm); and the SPWVT. The evaluation was performed on artificial data that have a typical pattern of nonstationary series and has documented the superiority of the SPWVT in the joint time-frequency domain.

SPWVT Compared With FFT

The frequency range for HRV power spectral analysis has been divided on the basis of the results of the FFT into three components: the very-low-frequency component (<0.04 Hz in humans), which has been eliminated from this study by filtering; the HF component (≈0.20 Hz); and the LF component (0.04 to 0.15 Hz). The spectrum obtained with the FFT is nothing other than the spectrum obtained with the Wigner-Ville transform averaged for 3 minutes, or a mean of the instant spectra obtained with the SPWVT during the period used to smooth the Fourier transform. Therefore, during the stationary period that precedes or follows tilt, it is not surprising to obtain with the SPWVT the same sort of results as those previously reported with the FFT or AR algorithms,[3923] ie, an acceleration of heart rate, a withdrawal of the HF oscillations, and an increased LF (both in normalized value), resulting in a pronounced augmentation of the LF/HF ratio (from 2 to 14 in Table 2, from 3 to 20 in Reference 9[9]). These results were basically the same in the two experimental groups despite the disparity between group 1 and 2 median ages. The only difference is that the values of RR variance and LF+HF sum in the supine position were not different from those characterizing the 90° position, in contrast to previous observations.[39] These discrepancies could be due to the method used to calculate the HRV spectra by parametric AR modeling (see Fig 5 in Reference 4[4]).

Determinants of the Sympathovagal Balance

The interpretation of the mechanisms involved in the genesis of the two main rhythmic components that can be identified in short temporal series (LF and HF) has been widely debated.[4] One of the hypotheses[27] is that they both originate from a complex central and peripheral interaction of sympathetic and parasympathetic mechanisms. Conversely, only a central push-pull organization between the two rhythms seems capable of explaining the functional significance of sympathetic and vagal modulation conveyed by the LF and HF components, respectively. Crucial, in this sense, is the observation that both LF and HF oscillations can be detected in the discharge variability of central brain-stem neurones of the cardiovascular regulatory areas.[28] More recently, it has also been demonstrated that the LF and HF oscillatory components that characterize the muscle sympathetic nerve discharge in normal human subjects undergo, during graded increases or decreases in blood pressure, reciprocal changes that were highly correlated with the corresponding values of blood pressure.[29] Our finding that on a time scale of one beat, the changes in heart rate, ICF, and amplitude of HF and LF were simultaneous is in full agreement with the above push-pull hypothesis.

An additional factor of complexity has recently been reported, the state of the myocardial adrenergic and muscarinic receptors.[717] In both experimental models of cardiac hypertrophy and transgenic technology, it has indeed been demonstrated that HRV is regulated not only by central or peripheral neural input but also by the β-adrenergic/muscarinic receptor density ratio. The two oscillatory components of the HRV disappear in a strain of transgenic mice in which the overexpression of the

β_1-adrenergic receptor has been targeted to the atria by use of the promoter sequence of the atrial natriuretic factor.[1730] Interestingly, such mice never suffer from arrhythmias and had an unaltered lifespan, strongly suggesting that the prognostic value of an attenuated HRV is linked to the presence of preexisting cardiac disease, whatever it is.

ICF to Explore the Sympathovagal Balance

The above considerations have already led to a proposal to analyze the activity of the autonomic nervous system by considering the sympathovagal balance instead of trying to arbitrarily separate one tone from the other.[372731] The LF/HF ratio and the use of normalized units are good approximations of the balance; nevertheless, they both have limitations based on the uncertainties concerning the limits of the two groups of oscillations and the fact that LF, and probably HF, have a mixed origin. In addition, the traditional spectral methodology has so far been based on mean values over a given length of time and afforded only the possibility of analyzing time series having some degree of stationarity. The ICF is likely to equally reflect the sympathovagal interaction. It is modified during tilt. In addition, it has the advantage of being a frequency measure independent of the arbitrary limits between HF and LF. The corresponding algorithm can be applied to the entire spectrum or restricted to a particular range of oscillations. ICF correlates with the LF/HF ratio (Fig 3); nevertheless, ICF correlates better with the heart rate, which is the gold standard, than the LF/HF ratio (Fig 4). The routine use of ICF necessitates careful sampling because the frequency ranges of the shift are ≈0.05 Hz (Table 2).

The SPWVT offers the possibility of assessing the dynamic changes of the sympathovagal interaction. As illustrated in Fig 4, during the transient phase of the tilt, ICF and the spectral power amplitude were modified simultaneously. The concept of a sympathovagal balance is then again verified in dynamic conditions but on the basis of a different set of assumptions. In fact, the only prerequisite to our interpretation of data was that a frequency shift of ICF indicates a change in sympathetic activity. The whole of the results strongly indicates that sympathetic excitation corresponds to a decrease in ICF. In general, it is not surprising that an oscillatory phenomenon might possess a true code of frequency that might be more sensitive during transients. In contrast, the power amplitude might rather reflect stationary conditions.

Clinical Applications

The instant transform methods allow quantification of transients in term of spectral power nearly every second and as such are particularly appropriate tools to study transitions. Fig 4 illustrates the sensitivity of the technique. The method provides information, on this scale, on the amplitude of the power spectrum, its period, and also on the ICF. Nevertheless, the method also showed the extreme variability of the spectrum both in terms of power and ICF (Figs 1 and 4). In fact, the spectrum power is much more variable when plotted against time than frequency, suggesting that the biological regulation is done primarily at the level of a frequency shift toward lower or higher frequencies, as already suggested by neurophysiological studies. Numerous potential clinical applications can be proposed. ICF is a new tool to explore the prognostic significance of the HRV, and the tool correlates better with heart rate, which also has a prognostic significance,[3233] and may improve the detection of such a risk stratification. The SPWVT, as an instant method of spectral analysis, could be more accurately proposed to study the transition period before episodes of malignant arrhythmias, atrial fibrillation, or vagal syncopes to more properly assess the sympathovagal balance.

Selected Abbreviations and Acronyms

AR	=	autoregressive
FFT	=	fast Fourier transformation
HF	=	high frequency
HRV	=	heart rate variability
ICF	=	instant center frequency
LF	=	low frequency
SPWVT	=	smoothed pseudo–Wigner-Ville transform

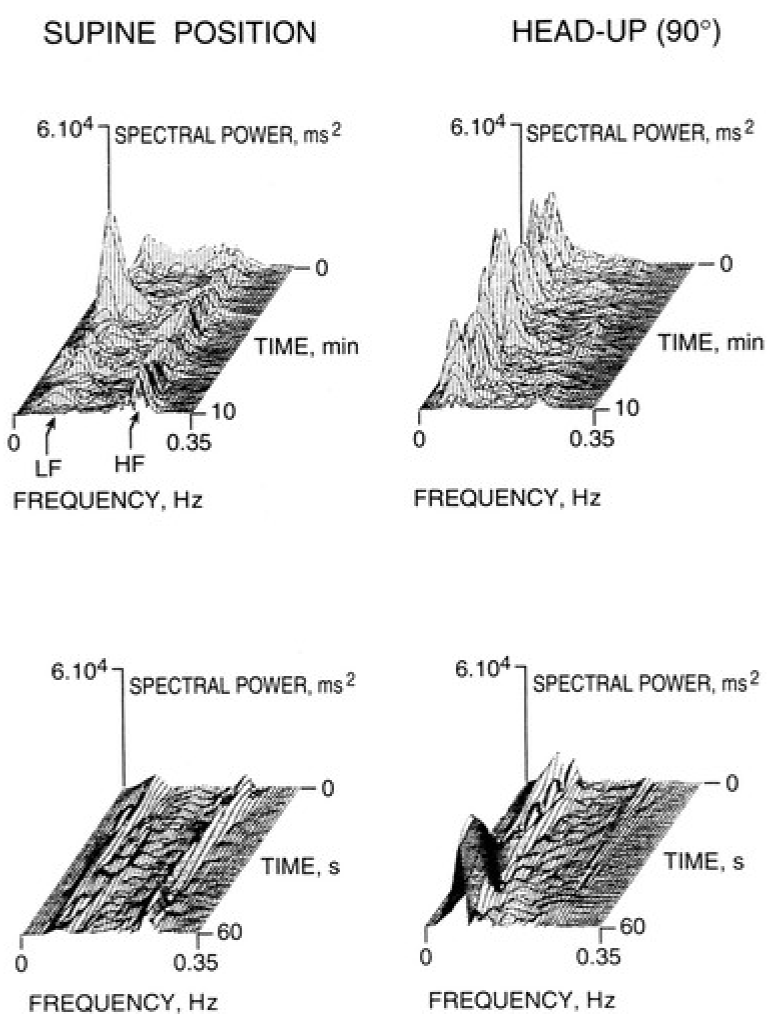

Figure 1. Instant time-/frequency-domain analysis (SPWVT) of heart rate during tilt test. Typical 3D representation in healthy volunteer under metronome breathing at 0.25 Hz. Holter monitoring. Inclination of table was set at 90° after 20 minutes in supine position (group 2). 3D representation shows, on two different time scales, spectral power (in ms^2) of HRV during first 10 minutes (top left) or first minute (bottom left) in supine position and during last 10 minutes (top right) or last minute (bottom right) in head-up position. Very-low-frequency oscillations were eliminated by previous filtering. Large peaks on left in LF area represent LF oscillations.

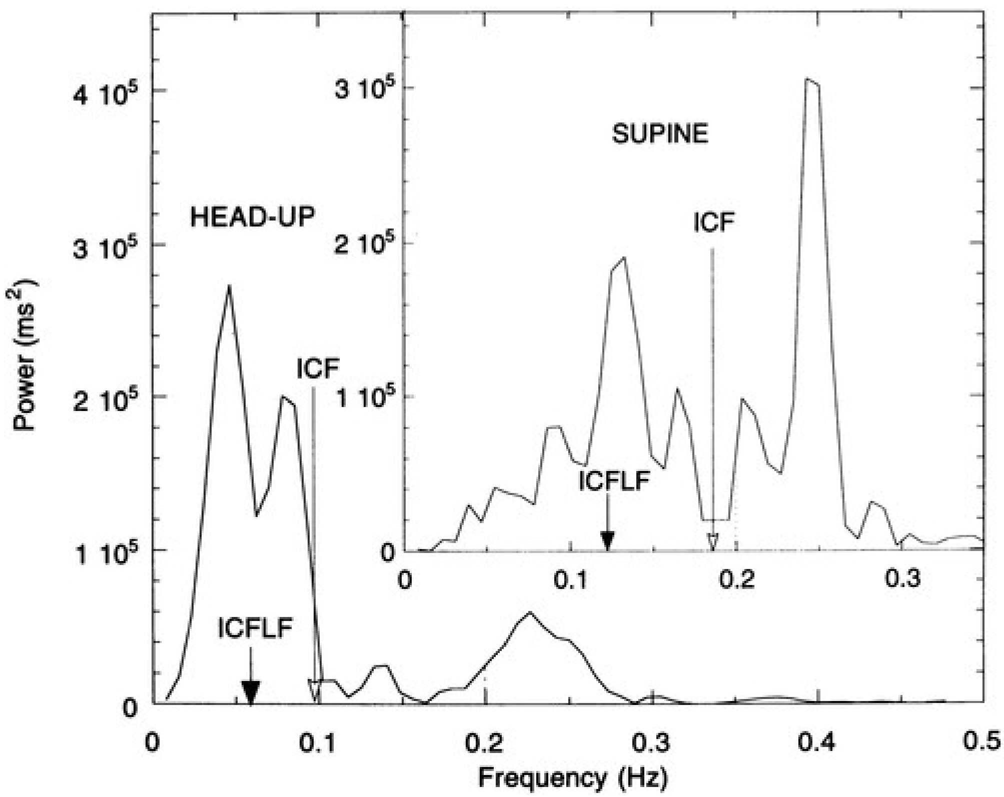

Figure 2. Time-/frequency-domain analysis of heart rate during tilt. Instant spectrum in supine (inset) and head-up positions. Typical example in healthy volunteer under metronome breathing at 0.25 Hz (group 2). Vertical lines represent, in Hz, ICF of whole spectrum and ICF of LF oscillations (ICFLF).

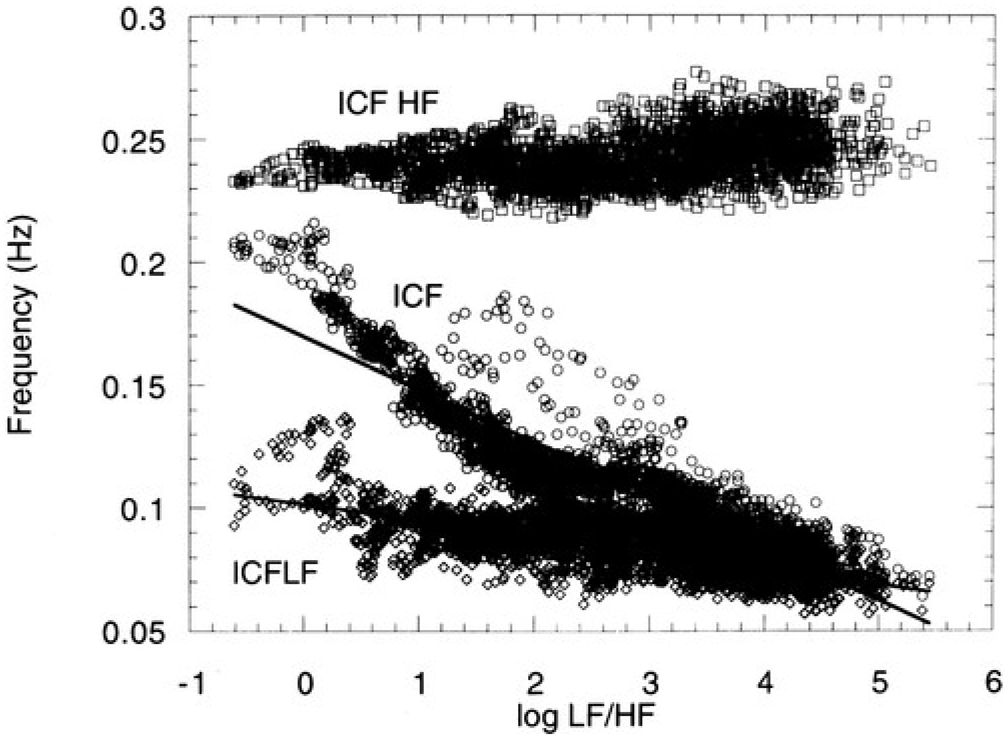

Figure 3. Time-/frequency-domain analysis of heart rate during tilt. Correlations between log LF/HF ratio and ICF of whole spectrum (circles, ICF, r=.88, P<.001) of LF (diamonds, ICFLF, r=.68, P<.01) and HF (squares, ICFHF, r=.10, P=NS). LF/HF ratio does not correlate with ICFHF oscillations because subjects were under controlled breathing. Continuous Holter monitoring (group 2). One healthy volunteer; 2000 points were averaged, 1000 at rest and 1000 in head-up position (see Table 2).

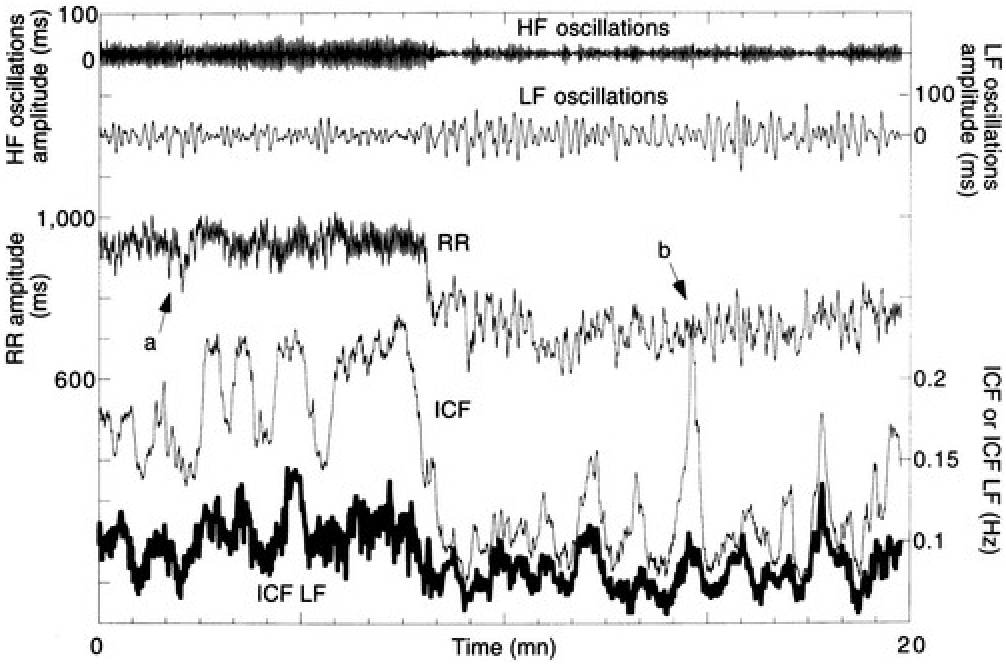

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Figure 4. Time-frequency analysis of heart rate during continuous tilt (group 2). Metronome breathing at 0.25 Hz. Typical example. Amplitude of oscillations was obtained by finite impulse response filtering. Top to bottom: amplitude of HF and LF (ms), RR interval (ms), and ICF (in Hz) of whole spectral power (ICF) and LF (ICF LF). Tilt between 7 and 8 minutes. a and b show that increased ICF coincides with increased frequency of heart rate oscillations.

Table 1. Random Tilt Test (Group 1) in Young and Mature Healthy Volunteers

RR interval	
Mean, ms	−0.57[3]
Variance, ms^2	−0.02
Spectral power, ms^2	
LF	0.03
HF	−0.28
LF/HF	0.39[2]
Spectral power, normalized units	

LF	0.39[2]
HF	−0.39[2]
ICF, Hz	
ICF of whole spectral power	−0.52[3]
ICF of LF	−0.29[1]

Power spectrum analysis using an instant time- and frequency-domain method, the SPWVT. Correlation coefficients between the angles of inclination of the table in degrees and the RR intervals or various parameters measuring heart rate and HRV.

[1]*P*<.05,

[2]*P*<.01,

[3]*P*<.001.

Table 2. Continuous Tilt Test (Group 2) in Healthy Volunteers

	Resting Position	Upright Position
RR interval		
Mean, ms	909±90	721±116[1]
Variance, ms^2	5148±4609	5437±6137
Spectral power, ms^2		
LF	773±626	956±928
HF	431 ±281	86±77[1]
Spectral power, normalized units		
LF	60 ±14	88±9[1]

	Resting Position	Upright Position
HF	39±14	11±9[1]
LF/HF	2.3 ±3.0	14.5±12.3[1]
ICF, Hz		
ICF of spectral power	0.15 ±0.02	0.10±0.02[1]
ICF of LF	0.10±0.01	0.08 ±0.01[1]

Power spectrum analysis using an instant time- and frequency-domain analysis, the SPWVT. Mean±SD of 1000 points collected during 7 minutes before the change of the angle (resting position) and 1000 points collected during 7 minutes after the change of the angle (upright position) and a short period of stabilization.

[1]*P*<.001.

Footnotes

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