Spectral Characteristics of Heart Rate Variability Before and During Postural Tilt Relations to Aging and Risk of Syncope

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Fourier analysis of heart rate (HR) may be used to characterize overall HR variability as well as low- and high-frequency components attributable to sympathetic and vagal influences, respectively. We analyzed HR spectral characteristics of 12 healthy young (18–35 years) and 10 healthy old (71–94 years) subjects before and during 60° head-up tilt. Total spectral power in the 0.01–0.40-Hz frequency range and low-frequency (0.06–0.10 Hz) and high-frequency (0.15–0.40 Hz) components of the HR power spectrum were significantly lower in old than in young subjects in supine and upright positions. To characterize and compare overall HR variability in young and old subjects, we computed the regression lines relating the log amplitude to the log frequency of the supine HR spectra (1/f plots). The regression lines for old subjects were lower and steeper (mean slope, −0.78 [5%, 95% confidence limits (CL), −0.73, −0.83]) than in young (mean slope, −0.67 [CL, −0.62, −0.72]), indicating not only reduced overall spectral amplitude but also relatively greater attenuation of high-frequency HR components in the old subjects. This finding illustrates a novel way to quantify the loss of autonomic influences on HR regulation as a function of age. During postural tilt, HR variability was unchanged in the old subjects. For the entire group of young subjects, total HR variability increased during tilt. Six young subjects developed vasovagal syncope during tilt, enabling us to examine differences in the HR spectra of these subjects while they were asymptomatic before syncope. Subjects with syncope had a significant increase in total and low-frequency HR variability during tilt, whereas those without syncope had no significant change in the HR spectrum. Thus, the old subjects have reduced supine HR variability and absent or attenuated low-frequency activation during tilt. Young subjects who develop syncope during tilt demonstrate prominent low-frequency activation, which may be associated with heightened sympathetic activity. Our findings may provide a physiological explanation for resistance to vasovagal syncope in old age. (Circulation 1990;81:1803–1810)

Heart rate and blood pressure responses to physiological perturbations—such as cough, respiration, the Valsalva maneuver, and postural change—have been used to assess autonomic nervous system function under healthy conditions, with certain diseases, and with aging. However, only limited information about autonomic control of heart rate can be obtained by traditional statistical measures based solely on changes in mean heart rate and variance.1,2 Therefore, increasing attention is being focused on quantifying various aspects of heart rate dynamics associated with beat-to-beat fluctuations. Spectral analysis is one useful technique for quantifying overall heart rate variability as well as specific components of this variability putatively associated with respiration, sympathetic nervous system activity, and other physiological influences.3–6

Spectral analysis reduces a signal (such as a heart rate time series) to its constituent frequency components and quantifies the relative power (squared amplitude) of these components.6,7 Under healthy conditions, heart rate is not strictly regular or periodic,


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Despite the connotations of the commonly used clinical term “regular sinus rhythm.” Instead, the heart rate in healthy subjects, even at rest, shows considerable beat-to-beat variability that is represented by a broadband spectrum with superimposed peaks due to physiological oscillations (Figure 1).

The highest frequency oscillations of heart rate (approximately 0.15–0.40 Hz) are exclusively due to vagal control and can be correlated with respiration (phasic sinus arrhythmia). Somewhat lower frequency oscillations of heart rate (approximately 0.06–0.1 Hz) appear to be an index of sympathetic activity. Even lower frequency spectral peaks associated with the renin-angiotensin system and other control mechanisms have been described by some investigators but are difficult to identify in human subjects.

In the present investigation, we used heart rate spectral analysis to help assess changes in autonomic function in two conditions: physiological aging and vasovagal syncope. These two conditions are of interest, because in some respects they appear to represent extremes of autonomic activity. Physiological aging is associated with a reduction in parasympathetic control of heart rate, demonstrated by a decline in respiratory sinus arrhythmia and a reduction in the bradycardic response to the Valsalva maneuver. In contrast, vasovagal syncope, which is more common in younger than in older individuals, is thought to reflect heightened parasympathetic influence on heart rate.

Previous work from our own laboratories has demonstrated a reduction in low-frequency heart rate fluctuations in elderly subjects. This is consistent with the known age-related decline in cardiac responsiveness to sympathetic activation. Thus, elderly individuals have a restricted range of sympathetic and parasympathetic responses to physiological stress, which may have important clinical implications. With regard to vasovagal syncope, a vigorous inotropic cardiac response to sympathetic stimulation can evoke reflex hypotension and bradycardia due to activation of afferent vagal fibers arising from the ventricular wall (the Bezold-Jarisch reflex). Reduced cardiac responsiveness to sympathetic activation or a decline in vagal tone may decrease the risk of vasovagal syncope in old age.

We addressed two interrelated questions in this study. 1) What is the effect of aging on sympathovagal balance, as determined by short-term heart rate variability, overall and in selected high- and low-frequency bands? 2) Do young subjects who are particularly susceptible to vasovagal syncope induced by postural tilt show any evidence of heightened autonomic activity compared with nonsyncopal subjects?

**Methods**

**Subjects**

Thirteen young and 11 old individuals volunteered to participate in the study. Before data analysis, one young subject (who developed syncope) was excluded because of technical problems during electrocardiographic (ECG) monitoring, and one old subject
(without syncope) was excluded because of frequent atrial premature beats. Therefore, data were analyzed from 12 young subjects (five women, seven men; median age, 21.5 years; range, 18–35 years) and 10 old subjects (six women, four men; median age, 76.5 years; range, 71–94 years). All subjects were screened with a careful history, physical examination, routine laboratory tests, and resting 12-lead ECG to ensure that they were in good health and without acute illnesses, clinically apparent cardiovascular disease, diabetes mellitus, or neurological disease. Subjects did not smoke cigarettes or take medications. The research protocol was approved by the institutional review boards of the Hebrew Rehabilitation Center for Aged and Beth Israel Hospital, and each subject gave informed consent.

Postural Tilt Protocol

Subjects were instructed to fast after midnight the night before the study. At 7:30 AM, with the subject supine on a tilt table, an intravenous catheter was inserted in a forearm vein for a simultaneous study requiring a 7–10-ml infusion of propranolol or saline. Data for the present study were obtained during the supine control phase, at least 25 minutes after intravenous catheter insertion and saline injection. Two ECG leads were recorded continuously with a tape recorder (Del Mar Avionics, Irvine, California). Critical events during the study were marked by an electrical signal on the tape. Forearm cuff blood pressure was measured at 5-minute intervals while the subject was supine and at 1, 3, and 6 minutes after the beginning of postural tilt with an automatic oscillometric blood pressure monitor (Critikon, Tampa, Florida).

After 1 hour of supine rest, the tilt table was inclined during a 10-second period to 60° head-up, kept in that position for 15 minutes, and then returned to the supine position. Subjects were supported by belts at the waist and knees and by a foot rest. If symptoms of impending syncope occurred during the tilt, the subject was immediately brought back to the supine position. Six of the young subjects developed vasovagal symptoms. In each such case, the onset of symptoms occurred after at least 6 minutes of tilt.

Heart Rate Spectral Analysis

Tape-recorded ECGs for each subject were digitally processed and annotated by manual editing with a Holter Analysis System (Series 8000, Marquette, Milwaukee, Wisconsin). We analyzed heart rate variability during the 5-minute period just before tilt during supine rest and during the 5-minute period immediately after tilt in the 60° head-up position while all subjects were asymptomatic.

The instantaneous heart rates during the 5-minute periods before and after tilt were resampled twice per second and processed by a fast Fourier transform algorithm yielding a 512-point spectrum for the 0.01–1.0-Hz frequency band. The direct current component was excluded from the power spectrum. We measured the total power ($P_T$, 0.01–0.40 Hz), the low-frequency band power ($P_L$, 0.06–0.10 Hz), and the high-frequency band power ($P_H$, 0.15–0.40 Hz). It is not possible to characterize frequency components of heart rate variability at frequencies above half the heart rate (corresponding to the Nyquist frequency for a uniformly sampled signal). As this critical frequency (approximately 0.5 Hz in our study) is approached, estimation error due to the low-pass filtering imposed by the resampling process becomes significant. For this reason, we only considered frequencies up to 0.4 Hz.

To characterize and compare overall heart rate variability in the young and old subjects and to minimize the effect of low-frequency noise on our analysis, we computed the slope of the regression line relating the log of spectral amplitude to the log of frequency. This regression is called a l/f plot because of the inverse relation between amplitude (or power) and frequency that characterizes spectra of this kind. This relation is illustrated in Figure 1 where the amplitude of heart rate spectral components varies inversely with their frequency. The absolute slope of the regression line equals the exponent $x$ in the l/f plot. This exponent can be used to characterize the overall distribution of frequencies and their amplitudes. It is also an index of the nonlinear (fractal) dimension of a process. Because we postulated that there is selectively greater loss of high-frequency heart rate variability in old than in young subjects, we anticipated a more negative slope for old subjects, that is, $x$ would be greater in the old than in the young subjects.

Statistical Analysis

A bootstrap-based statistical procedure was used to estimate 5% and 95% confidence limits (CL). This method was used because it does not rely on assumptions about the underlying sample distribution and is also effective in analyzing small data sets. Results are reported as mean±SD and as 5% and 95% CL. Differences were considered statistically significant if there was no overlap between the confidence limits.

Results

Mean Blood Pressure and Heart Rate Responses to Postural Tilt: Old and Young Subjects

Blood pressure responses to postural tilt are summarized in Table 1. At all points, blood pressure was higher in old than in young subjects. However, blood pressure did not change significantly in either group during tilt. As shown in Table 2, baseline heart rate was similar in young and old subjects. Although heart rate tended to increase to a greater extent in young than in old subjects during postural tilt, the difference was not significant.

Heart Rate Spectra: Old and Young Subjects

Representative heart rate time series and spectra for young and old subjects are shown in Figure 2 for
supine and tilt positions. The total power of heart rate variability was reduced in both positions in old compared with young subjects (Figure 2 and Table 3). In old compared with young subjects, marked reductions occurred in spectral power in the low- and high-frequency bands (Table 3).

During postural tilt, young subjects as a group demonstrated a significant increase in total power of heart rate variability, whereas old subjects did not. There was a tendency for the low-frequency bands to increase in young but not in old subjects. The high-frequency band remained unchanged in both groups.

Figure 3

l/f² Plots: Old and Young Subjects

The heart rate spectral frequency characteristics of each old and young subject are summarized in Figure 3 by l/f² plots of the log of heart rate frequency (x axis) and the log of the amplitude at each frequency (y axis). Comparison of these plots reveals two important differences between young and old subjects. First, the plots are consistently shifted downward in old subjects, demonstrating a reduction in total heart rate variability compared with young subjects. Second, the slopes of the l/f² plots of old (mean, −0.78 [CL, −0.73, −0.83]) are significantly steeper than the slopes of young subjects (mean, −0.67 [CL, −0.62, −0.72]), indicating a relatively greater attenuation of high-frequency heart rate variability in the old subjects. The scatterplot in Figure 3 provides another representation of the reduction in total spectral power and more negative slope of the l/f² plot in old than in young subjects.

Table 2: Heart Rate Responses of Young and Old Subjects in Supine and Tilt Positions

<table>
<thead>
<tr>
<th>Time</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young (n=12)</td>
</tr>
<tr>
<td>Before tilt</td>
<td>65±6</td>
</tr>
<tr>
<td></td>
<td>(59–72)</td>
</tr>
<tr>
<td>Tilt</td>
<td>77±8</td>
</tr>
<tr>
<td></td>
<td>(72–84)</td>
</tr>
</tbody>
</table>

Values are mean±SD; values in parentheses are 5–95% confidence limits. Each subject’s pretilt and tilt heart rate is the average obtained during a 5-minute period.

Table 3: Heart Rate Variability of Young and Old Subjects in Supine and Tilt Positions

<table>
<thead>
<tr>
<th>Frequency band</th>
<th>Young (n=12)</th>
<th>Old (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pₐ</td>
<td>1.34±0.84</td>
<td>0.30±0.16</td>
</tr>
<tr>
<td></td>
<td>(0.99–1.72)</td>
<td>(0.22–0.38)</td>
</tr>
<tr>
<td>Pₜ</td>
<td>1.27±1.07</td>
<td>0.19±0.09</td>
</tr>
<tr>
<td></td>
<td>(0.85–1.81)</td>
<td>(0.14–0.23)</td>
</tr>
<tr>
<td>Pₜ</td>
<td>10.02±4.49</td>
<td>3.14±2.25</td>
</tr>
<tr>
<td></td>
<td>(8.03–12.07)</td>
<td>(2.08–4.23)</td>
</tr>
<tr>
<td>Tilt</td>
<td>2.44±1.69</td>
<td>0.26±0.22</td>
</tr>
<tr>
<td></td>
<td>(1.66–3.26)</td>
<td>(0.16–0.38)</td>
</tr>
<tr>
<td>Pₜ</td>
<td>1.11±0.71</td>
<td>0.19±0.13</td>
</tr>
<tr>
<td></td>
<td>(0.80–1.45)</td>
<td>(0.13–0.25)</td>
</tr>
<tr>
<td>Pₜ</td>
<td>18.90±12.47</td>
<td>2.59±2.21</td>
</tr>
<tr>
<td></td>
<td>(12.95–24.76)</td>
<td>(1.61–3.72)</td>
</tr>
</tbody>
</table>

Values are mean±SD; values in parentheses are 5–95% confidence limits. Power is given in arbitrary units.

Heart Rate Spectra of Young Subjects With and Without Syncope

Six young subjects (four men and two women) developed characteristic symptoms of vasovagal syncope between 6 and 13 minutes of postural tilt, with sudden onset of dizziness, pallor, nausea, warmth, and diaphoresis, followed by relative bradycardia and hypotension. This provided the opportunity to stratify young subjects by their predisposition to vasovagal syncope and to compare supine and upright heart rate spectral frequency patterns of those with and without the subsequent development of vasovagal symptoms.

As shown in Table 4, young subjects who developed syncope had significant increases in low-frequency and total power during postural tilt, whereas those without syncope did not. Thus, the increase in low-frequency and total spectral power that was observed in the entire group of young subjects during tilt was due primarily to the contribution of subjects prone to syncope. The mean heart rate during the first 5 minutes of tilt (before syncope) in the six syncopal subjects tended to be higher (83±9 [CL, 72, 93] beats/min) than in the six nonsyncopal subjects (72±7 [CL, 69, 76] beats/min); however, the overlapping confidence limits indicate that this difference was not significant.

Young subjects without syncope had significantly greater total spectral power while supine than those who developed syncope. However, supine low- and high-frequency powers did not differ between the two groups (Table 4).

Discussion

This study has several new findings that extend previous observations on the dynamics of heart rate...
variability in different physiological contexts. First, our data confirm the reduction in overall supine and upright heart rate variability in healthy old compared with young subjects but also demonstrate that this reduction occurs in high- as well as low-frequency components of the heart rate spectrum. To our knowledge, this is the first demonstration that higher frequency heart rate fluctuations, representing vagal influences, are selectively more attenuated in advanced age. Second, our data suggest that young subjects who develop syncope during postural tilt have heightened sympathetic activation that may predispose them to vasovagal syncope. Last, the present study quantified the spectral alteration in heart rate variability in advanced age with a novel technique based on \( \frac{I}{f^4} \) plots.\textsuperscript{21,26,27} From a physiological perspective, the use of \( \frac{I}{f^4} \) plots is of interest, because the method suggests a simple way to quantify the loss of dynamic range in a complex system as it ages.

**Heart Rate Spectral Characteristics in Advanced Age**

To our knowledge, only two previous studies have used spectral analysis techniques to examine changes in components of heart rate variability in subjects older than 65 years.\textsuperscript{15,16} The reduction in total heart rate variability observed in our old subjects is in agreement with a previous report by Simpson and Wicks.\textsuperscript{16} However, in contrast to their findings, we were unable to demonstrate any increase in low-frequency (predominantly sympathetic) modulation of heart rate in old subjects during postural tilt. Because their study protocol differed from ours in allowing a 2-minute adjustment period to upright posture before 6 minutes of heart rate monitoring, it

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**FIGURE 2.** Heart rate time series (top panel) and frequency spectra (bottom panel) in one young and one old subject in supine and tilt positions. In the time series plots, note the increased heart rate fluctuations in the young compared with the old subject in both positions. As shown in the spectral plots, the young subject demonstrates an increase in the low-frequency component (0.06–0.10 Hz) during tilt, whereas the old subject does not. Spectral amplitude is given in arbitrary linear units.
is possible that activation of low-frequency components of heart rate variability is delayed in old subjects. Also, the difference in mean age of subjects (80 years in our study and 68 years in their study) suggests that recruitment of low-frequency heart rate oscillations during tilt may further diminish in far advanced age. Our observations are supported by previous work in our laboratory demonstrating loss or marked attenuation of low-frequency oscillations (Mayer-like waves) in healthy old subjects (65–84 years) exposed to 3 minutes of tilt.

Our study also demonstrated that higher frequency heart rate oscillations are disproportionately attenuated in very old subjects. Pagani et al also examined supine and post-tilt heart rate oscillations as a function of age. They reported an age-related decline in total RR interval variance but no significant alteration in the ratio of low- to high-frequency components of heart rate variability. However, none of their subjects was older than 60 years. It is possible that alterations in spectral characteristics of heart rate variability may occur relatively abruptly, rather than progressively, after age 60 years. The reduction in high-frequency components of heart rate variability observed in our study is consistent with the known effects of aging on vagal control of the respiratory sinus arrhythmia and bradycardic response to the Valsalva maneuver.

**Heart Rate Spectral Characteristics of Subjects With Syncope**

Our results also suggest that the recruitment of low-frequency heart rate oscillations during postural tilt is not uniform among all young subjects and that more prominent low-frequency activation may indicate a predisposition to vasovagal syncope. The fact that, on average, the small group of nonsyncopal young subjects tended to have increased low-frequency and decreased high-frequency oscillations during tilt, as has been shown in previous studies, suggests that our small sample size did not permit us to detect significant changes in this group. However, the magnitude of low-frequency activation in the syncopal subjects was greater than that in the asymptomatic group. Previous studies that report an increase in low-frequency heart rate oscillations in healthy young subjects during tilt do not comment on the interindividual variability of this response or on the development of syncopal symptoms in their subjects. It is possible that the subjects of previous studies who
showed low-frequency activation during tilt would have experienced syncope if they were studied during longer periods of tilt or in the fasting state.

Although our finding of enhanced low-frequency activation in syncopal subjects is a preliminary observation based on a small sample size, there are at least two lines of supporting evidence. First, vasovagal syncope has been shown to be preceded by sympathetic nervous system activation as demonstrated in one study by elevated levels of plasma catecholamines at the time of vasovagal symptoms in five subjects and in another study by an increase in sympathetic vasoconstrictor impulses recorded with microelectrodes in peroneal nerve fascicles before vasovagal syncope in two subjects. Also, a recent abstract reported findings similar to ours with spectral analysis techniques. In this study, 12 healthy young champion swimmers with postural tilt-induced vasovagal syncope had a higher amplitude of low-frequency heart rate oscillations during tilt and before syncope than 22 other swimmers without syncope. However, tilt-induced changes in the heart rate spectrum were not reported.

A second set of observations in support of our findings suggest that sympathetic activation during postural tilt may produce vasovagal syncope by precipitating the Bezold-Jarisch reflex. Mark and Simple et al. summarized data suggesting that with decreased venous blood return to the heart and associated sympathetic activation that occurs during upright tilt, vigorous cardiac contraction around a relatively hypovolemic ventricle can trigger reflex bradycardia and vasodilation (Bezold-Jarisch reflex), resulting in vasovagal syncope. In old subjects, decreased baroreflex sensitivity, decreased cardiac responsiveness to β-adrenergic stimulation, and decreased parasympathetic influence on the heart (suggested by the present study) may prevent activation of this reflex during tilt.

Heart Rate Dimensionality, Aging, and l/f-Like Spectra

Healthy individuals, particularly young subjects, exhibit considerable beat-to-beat variability in sinus rhythm even at supine rest (Figure 1). This variability that spans multiple orders of temporal magnitude is apparently due to nonlinear interactions of sympathetic and parasympathetic influences on the sinus node.

Previous analyses of the effect of aging on heart rate variability have been restricted to examination of spectral amplitude in selected frequency bands or have used conventional measures of variance. The l/f plots used in this study are attractive, because they enable comparison of the overall heart rate spectrum under different conditions. In particular, the l/f statistic not only permits assessment of absolute spectral amplitude (or power) for the multiple frequency components of broadband spectra, but it also provides a simple quantitative way of evaluating the relative amplitudes of higher and lower frequency components.

Using this method, we have shown that 1) overall heart rate variability is reduced with advanced age (downward shift of regression line of old vs. young), and 2) high-frequency fluctuations are relatively more attenuated with advanced age (more negative slope of the regression line for old vs. young) (Figure 3). These spectral alterations with aging are reminiscent of the dynamics of presbycusis in which high-frequency hearing is selectively impaired with aging.

Recently, it was postulated that the kind of broadband variability seen in healthy heart rate fluctuations, and represented by a l/f-like spectrum, may be due to a fractal mechanism. The fractal concept applies to certain kinds of complex nonlinear processes that do not have a single scale of time (i.e., a single-frequency component). The exponent x of the l/f distribution that gives the slope of the l/f regression line can be used to provide a crude estimate of the so-called fractal dimension of a nonlinear process. This kind of dimension can be conceptualized as a measure of the complexity of the process.

As a nonlinear process loses its complexity, its dimension decreases. This reduction in dimensionality will correlate with a more negative slope of the l/f plot that characterizes the process. We hypothesized that advanced age would be associated with a loss of dimensionality due to reduced autonomic responsiveness. Our finding that aging shifts the l/f slope of heart rate more negatively is consistent with this prediction.

Potential Limitations and Future Studies

Although our data provide potentially important information about changes in spectral characteristics of heart rate variability in healthy very old individuals and in young subjects with tilt-induced syncope, they are limited by a small sample size. Also, our data show greater variability among young subjects than suggested in previous studies. However, previous investigations do not characterize interindividual differences in heart rate frequency spectra. Furthermore, young subjects in previous studies were predominantly male. Additional studies are needed, therefore, to confirm the present findings and to explore possible differences in heart rate variability, supine and during tilt, among subsets of healthy subjects stratified by age as well as gender.

A potential limitation of spectral analysis techniques for the evaluation of responses to physiological perturbations such as postural tilt is that nonstationary conditions may increase noise in the data. Therefore, the fast Fourier transform must be interpreted cautiously. We were careful to include heart rate data during the 5-minute period before the development of vasovagal syncope while all subjects were asymptomatic. Because the identical tilt protocol was applied to each subject, intergroup comparisons of spectral characteristics should give valid
information about different patterns of response to orthostatic stress.

Last, although our data suggest that young subjects with tilt-induced syncope have enhanced low-frequency heart rate oscillations shortly before fainting, we were unable to predict the risk of syncope based solely on their 5-minute pretilt data samples. Perhaps Fourier analysis of data for longer periods of supine heart rate time series will provide such a spectral marker of susceptibility to vasovagal syncope related to lower frequency fluctuations associated with sympathetic control. Alternatively, standardization of respiratory rate with metronomic breathing may help unmask subtle differences in higher frequency oscillations associated with alterations in vagal control.

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References


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