American Journal of Physiology – Heart and Circulatory Physiology

Comparison of spontaneous vs. metronome-guided breathing on assessment of vagal modulation using RR variability

Daniel M. Bloomfield, Anthony Magnano, J. Thomas Bigger, Jr., Harold Rivadeneira, Michael Parides and Richard C. Steinman

AJP - Heart 280:1145-1150, 2001.

You might find this additional information useful...

This article cites 15 articles, 12 of which you can access free at:
http://ajpheart.physiology.org/cgi/content/full/280/3/H1145#BIBL

Medline items on this article's topics can be found at http://highwire.stanford.edu/lists/artbytopic.dtl on the following topics:
Medicine .. Heart Diseases
Medicine .. Risk Factors
Medicine .. Respiration

Updated information and services including high-resolution figures, can be found at:
http://ajpheart.physiology.org/cgi/content/full/280/3/H1145

Additional material and information about ***AJP - Heart and Circulatory Physiology*** can be found at:
http://www.the-aps.org/publications/ajpheart

This information is current as of November 5, 2005 .

AJP - Heart and Circulatory Physiology publishes original investigations on the physiology of the heart, blood vessels, and lymphatics, including experimental and theoretical studies of cardiovascular function at all levels of organization ranging from the intact animal to the cellular, subcellular, and molecular levels. It is published 12 times a year (monthly) by the American Physiological Society, 9650 Rockville Pike, Bethesda MD 20814-3991. Copyright © 2005 by the American Physiological Society. ISSN: 0363-6135, ESSN: 1522-1539. Visit our website at http://www.the-aps.org/.

Downloaded from ajpheart.physiology.org on November 5, 2005

Am J Physiol Heart Circ Physiol
280: H1145–H1150, 2001.

Comparison of spontaneous vs. metronome-guided breathing on assessment of vagal modulation using RR variability

DANIEL M. BLOOMFIELD,[1] ANTHONY MAGNANO,[1] J. THOMAS BIGGER, JR.,[1] HAROLD RIVADENEIRA,[1] MICHAEL PARIDES,[2] AND RICHARD C. STEINMAN[1]
[1]*Division of Cardiology, Department of Medicine, and* [2]*Department of Biostatistics, School of Public Health, Columbia University, New York, New York 10032*

Received 6 August 1999; accepted in final form 18 October 2000

Bloomfield, Daniel M., Anthony Magnano, J. Thomas Bigger, Jr., Harold Rivadeneira, Michael Parides, and Richard C. Steinman. Comparison of spontaneous vs. metronome-guided breathing on assessment of vagal modulation using RR variability. *Am J Physiol Heart Circ Physiol* 280: H1145–H1150, 2001.—R-R interval variability (RR variability) is increasingly being used as an index of autonomic activity. High-frequency (HF) power reflects vagal modulation of the sinus node. Since vagal modulation occurs at the respiratory frequency, some investigators have suggested that HF power cannot be interpreted unless the breathing rate is controlled. We hypothesized that HF power during spontaneous breathing would not differ significantly from HF power during metronome-guided breathing. We measured HF power during spontaneous breathing in 20 healthy subjects and 19 patients with heart disease. Each subject's spontaneous breathing rate was determined, and the calculation of HF power was repeated with a metronome set to his or her average spontaneous breathing rate. There was no significant difference between the logarithm of HF power measured during spontaneous and metronome-guided breathing [4.88 ± 0.29 vs. 5.29 ± 0.30 ln(ms^2), $P = 0.32$] in the group as a whole and when patients and healthy subjects were examined separately. We did observe a small (9.9%) decrease in HF power with increasing metronome-guided breathing rates (from 9 to 20 breaths/min). These data indicate that HF power during spontaneous and metronome-guided breathing differs at most by very small amounts. This variability is several logarithmic units less than the wide discrepancies observed between healthy subjects and cardiac patients with a heterogeneous group of cardiovascular disorders. In addition, HF power is relatively constant across the range of typical breathing rates. These data indicate that there is no need to control breathing rate to interpret HF power when RR variability (and specifically HF power) is used to identify high-risk cardiac patients.

heart rate variability; power spectral analysis; parasympathetic nervous system; R-R interval

RECOGNITION THAT THE RESPIRATORY sinus arrhythmia was mediated by efferent vagal activity acting on the sinus node led investigators to attempt to quantify the fluctuations in R-R intervals that were related to breathing. Power spectral analysis of R-R intervals permits calculation of the amount of variance of a signal at a given frequency. Given that vagal modulation of sinus node activity occurs at the respiratory frequency (the respiratory sinus arrhythmia), measuring the variance (or power) in the R-R interval time series at the respiratory frequency provides a pure index of how much the vagus is modulating sinus node activity. We measure high-frequency (HF) power as the area under the power spectral curve between 0.15 and 0.40 Hz (quantifying the respiratory sinus arrhythmia with breathing rates of 9–24 breaths/min) given that the majority of subjects have breathing rates between 10 (0.17 Hz) and 20 (0.33 Hz) breaths/min.

However, a point of debate is whether vagal modulation is equivalent during spontaneous breathing and controlled breathing, such as with a metronome (6). During spontaneous breathing, breath-to-breath variation in the breathing rate causes HF power to be spread out over a frequency range. During metronome-guided breathing, there is little variation in the breathing rate, and HF power is confined to a narrow peak at the respiratory frequency. The recommendation that it is necessary to control breathing rate to accurately measure vagal modulation using HF power (6) has important implications for the use of R-R interval variability (RR variability) for physiological studies and clinical evaluations (where metronome-guided breathing can be cumbersome or even impossible) and thus deserves further evaluation.

Given that one of the most common and important uses of RR variability is to identify patients at increased risk of cardiovascular morbidity and mortality (16), we sought to evaluate the effect of metronome breathing on HF power in normal subjects and in patients with heart disease. This study design permits an assessment of the clinical significance of the effect of metronome breathing on HF power in the context of distinguishing high- and low-risk patients.

METHODS

Subjects. Informed written consent was obtained from all patients and healthy subjects. The study was approved by

Address for reprint requests and other correspondence: D. M. Bloomfield, College of Physicians and Surgeons, PH 3-342, 630 West 168th St., New York, NY 10032.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

 0363-6135/01 $5.00 Copyright © 2001 the American Physiological Society

American Journal of Physiology – Heart and Circulatory Physiology

Downloaded from ajpheart.physiology.org on November 5, 2005

the Columbia-Presbyterian Medical Center Institutional Review Board. A total of 45 subjects were recruited, although 6 study participants were excluded because of inability to complete the protocol ($n = 2$), tape malfunction ($n = 3$), and discovery of systemic disease in the healthy control group ($n = 1$).

Experimental protocol. Studies were performed in the supine position in a quiet room. The electrocardiogram (ECG) was monitored on an oscilloscope and continuously recorded on a Holter recorder for the duration of the study. An elastic respiratory belt (Pneumotrace respiration transducer model 1130, UFI, Morro Bay, CA) was secured around the subject's chest to measure breathing rate. The ECG and changes in thoracic circumference were recorded using a digital acquisition analysis program (Ponemah, version 1.21, Gould, Valley View, OH). Breathing rates were measured by computer and overread manually during the study.

Study procedures. Subjects were allowed to acclimate to their environment during a 10-min rest period. HF power, a measure of RR variability, was measured during this rest period. Each subject's average spontaneous breathing rate was measured and then programmed into a digital metronome. Subjects were instructed to breathe for 7 min, guided by the metronome at their average spontaneous breathing rate, while the measurement of HF power was repeated. In the second part of our study, we evaluated HF power during a randomized sequence of metronome-set breathing rates (6, 9, 10, 12, 14, 16, 18, and 20 breaths/min) for 7 min each. HF power was determined during each of these additional metronome-guided segments.

Analysis of Holter ECG recordings. All Holter tapes (~1.5-h duration) were analyzed with a scanner (model 8000, Marquette) running the Marquette analysis program (version 5.8) to identify and label each QRS complex. After the computer had automatically detected and labeled each QRS complex, a frequency histogram of the normal R-R (*N-N*) intervals was displayed, and the ECGs of the intervals in both tails of the *N-N* distribution were reviewed by a technician. After they were edited, the labeled QRS data stream was moved by means of a high-speed interface to a Sun 4/75 microcomputer, where a second stage of editing was performed using algorithms developed at Columbia University to find and correct any remaining QRS labeling errors that adversely affect measurement of RR variability.

Power spectral analysis of N-N intervals. Power spectral analysis of RR variability can be used to quantify parasympathetic modulation of sinus node activity. We computed R-R interval power spectra on the final 5-min segment of each 7-min segment of the study. The methods used for spectral analysis have been described previously (2, 5). A continuous function was derived from the discrete *N-N* intervals, filtered, and then sampled at 1,024 samples per 5-min segment to produce a time series for spectral analyses. The average *N-N* interval was subtracted from the time series, and a fast Fourier transform was performed to resolve the frequency components of cyclic activity in the time series of *N-N* intervals. Because the average *N-N* interval was subtracted from the time series of *N-N* intervals, changes in average *N-N* interval between different treatment periods should not affect the power spectral analyses.

Total power between 0.003 and 0.40 Hz was calculated. This approximates the total variance of the signal for a 5-min interval. Power in two bands of this power spectrum were quantified: 0.15–0.40 Hz (HF power) and 0.04–0.15 Hz [low-frequency (LF) power]. HF power is a pure parasympathetic signal reflecting respiratory sinus arrhythmia (1, 13); LF power reflects sympathetic and parasympathetic modulation of R-R intervals and is strongly influenced by baroreflex activity (1, 12, 13).

Statistical analysis. The replicate measures allowed each subject to serve as his or her own control. HF power was transformed to its natural logarithm for statistical analysis because of its positively skewed distribution. The logarithmic transformation succeeded in producing approximately normal distributions and thus allowed the use of parametric statistics. Values are means ± SE unless otherwise stated.

t-Tests were used to assess the statistical significance of differences for HF power under spontaneous and metronome-guided breathing at the same rate. The effects of the rate of metronome-guided breathing, presence of heart disease, and their interaction on the natural logarithm of HF power were examined using repeated-measures ANOVA. We adopted a univariate approach to the repeated-measures analysis, adjusting the degrees of freedom for the tests of the effect of metronome-guided breathing rate and its interaction with group with the Geiser-Greenhouse correction (9). In addition, we estimated the slope of the natural logarithm of HF power on metronome-guided breathing rate for each subject and assessed through least-squares regression the relationship between these slopes and metronome-guided breathing rate adjusting for presence or absence of heart disease. To determine whether the relationship between HF power and metronome-guided breathing rate is affected by the baseline spontaneous breathing rate, we also included the baseline rate of spontaneous breathing (in one model as a continuous variable and in another model dichotomized at 16 breaths/min) in the regression analyses.

On the basis of expectations for the mean HF power and its standard deviation from pilot data, we determined prospectively that a sample size of 40 subjects would provide >80% power at $\alpha = 0.05$ for detecting a 10% increase in the mean of the logarithm of HF power (based on mean = 6.5 units and SD = 1).

RESULTS

Characteristics of the subjects. Of the 39 subjects included in the study, 19 were patients with cardiac disease and 20 were healthy adults. Of the 19 cardiac patients, 15 were men and 4 were women, with a mean age of 59 ± 11 yr. All patients had supporting clinical and laboratory documentation of cardiac disease: 58% known coronary artery disease, 58% reduced ejection fraction, and 32% hemodynamically significant valvular disease. We excluded subjects with atrial fibrillation, pacemakers, extensive atrial or ventricular ectopy, or known peripheral neuropathic disorders. Of the 20 healthy subjects, 10 were men and 10 were women, with a mean age of 32 ± 11 yr. None of the healthy subjects had known cardiovascular or other systemic disease, and none was receiving medications.

Comparison of healthy subjects with cardiac patients. As expected, cardiac patients had significantly lower HF power than healthy subjects [3.55 ± 1.27 vs. 6.14 ± 1.31 (SD) $\ln(ms^2)$, $P < 0.0001$]. As a group, the cardiac patients were significantly older than healthy subjects, but the difference in HF power between healthy subjects and cardiac patients was much greater than the expected decline in HF power with age (4).

Spontaneous vs. metronome-guided breathing. Mean spontaneous breathing rates were 18.9 ±0.95 and 14.5

American Journal of Physiology – Heart and Circulatory Physiology

Downloaded from ajpheart.physiology.org on November 5, 2005

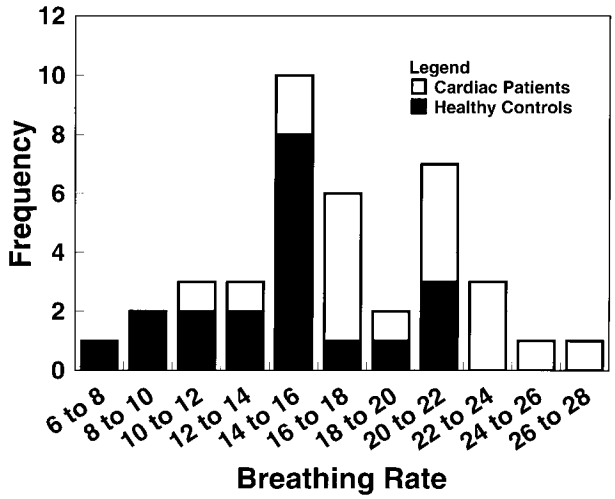

Fig. 1. Histogram of spontaneous breathing rates for the 39 subjects in the study.

±0.90 breaths/min for patients and healthy subjects, respectively (Fig. 1). There was no significant difference between HF power measured during spontaneous breathing and during metronome-guided breathing in the group as a whole or when patients and healthy subjects were examined separately (Fig. 2). The mean difference in the logarithm of HF power between spontaneous and metronome-guided breathing was -0.42 ± 0.94 ln(ms^2), which was not significantly different from zero ($P = 0.32$). Even though there was no significant difference in HF power when subjects were breathing spontaneously or with a metronome, the shape of the power spectrum did change during metronome-guided breathing (Fig. 3). When the subjects breathe spontaneously, the HF power spectrum is broader, because there is greater variability in the

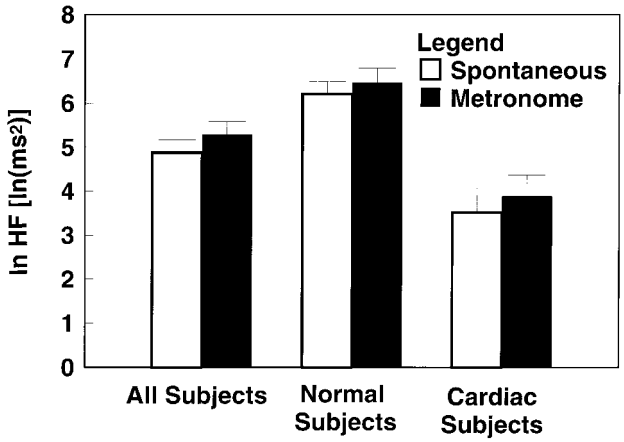

Fig. 2. Comparison of mean values for the logarithm of high-frequency (HF) power measured while subjects were breathing spontaneously and while subjects were breathing according to a metronome set to their average spontaneous breathing rate. Mean values are presented for the entire group and separately for healthy subjects and for patients with heart disease. The differences in HF between spontaneous and metronome-guided breathing are extremely small, especially compared with the large differences between HF power in healthy subjects and patients with heart disease.

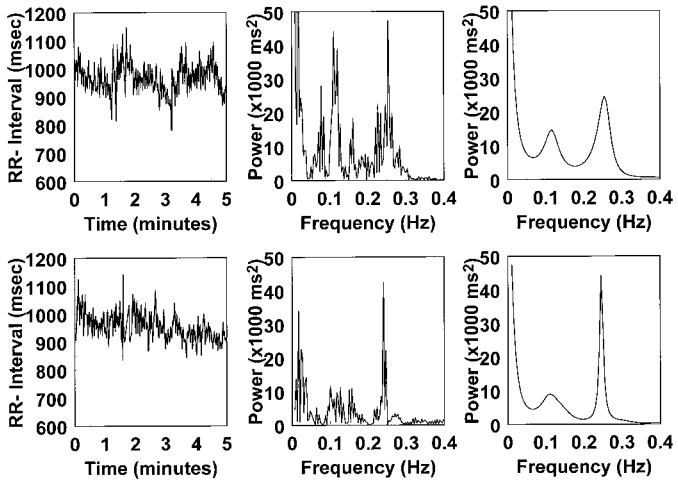

Fig. 3. Comparison of spontaneous (*top*) and metronome-guided breathing (*bottom*) from data from 1 healthy subject with a breathing rate of 15 breaths/min (0.25 Hz). R-R interval tachograms are displayed for 5 min (*left*), and corresponding power spectra are presented (*middle* and *right*). *Middle*: actual fast Fourier transform from which all calculations were made. *Right*: an autoregressed power spectrum, which is shown to facilitate the visual appreciation of the power spectra. During spontaneous and metronome-guided breathing, the HF power peak occurs at the same frequency, because the mean breathing rates are identical during these 2 type of breathing. However, the shapes of the 2 spectra are different: the HF peak during spontaneous breathing is broader, representing greater variability in the breath-to-breath interval. Because the variability in the breath-to-breath interval is significantly reduced during metronome-guided breathing, the HF power peak is narrower. The magnitude of HF power (the area under the curve between 0.15 and 0.40 Hz) in these 2 conditions is similar, and the effect of disease is much greater than the effect of metronome-guided breathing.

breath-to-breath interval. The variability in the breath-to-breath interval is significantly reduced when the subject's breathing is guided by a metronome, and the HF peak is correspondingly narrower.

There appeared to be greater HF power during metronome-guided than during spontaneous breathing (the mean difference is negative), which may have been related to larger tidal volumes associated with metronome-guided breathing. We did not measure tidal volume quantitatively. However, we did monitor changes in thoracic circumference with a strain gauge, which provides an index of tidal volume. In Fig. 4, changes in thoracic circumference using the strain gauge are displayed for a subject in whom HF power was greater during metronome than during spontaneous breathing. Even though the breathing rate was similar for both stages, the depth of breathing appeared greater during metronome-guided breathing than during spontaneous breathing.

Effect of breathing rate on HF power. To assess the effect of metronome-guided breathing rates on HF power, we examined HF power over the expected range of normal breathing rates (9–20 breaths/min) that are reflected by HF power in the frequency range of 0.15–0.40 Hz. HF power decreased from 5.84 ±0.30 ln(ms^2) at a breathing rate of 9 breaths/min to 5.26 ±0.26 ln(ms^2) at 20 breaths/min (Fig. 5). Using repeated-measures ANOVA, we controlled for the presence of

American Journal of Physiology – Heart and Circulatory Physiology

Downloaded from ajpheart.physiology.org on November 5, 2005

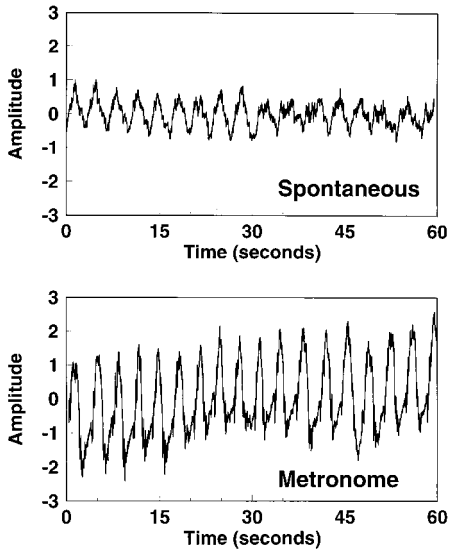

Fig. 4. Change in thoracic circumference estimated by a strain gauge during spontaneous and metronome-guided breathing. Depth of breathing appears greater during metronome-guided than during spontaneous breathing.

heart disease, since it had a large effect on HF power independent of breathing rate ($F_{1,37} = 49.89$, $P < 0.001$). This repeated-measures ANOVA of all subjects, controlling for the presence of heart disease, indicated a significant decrease in HF power with increasing metronome-guided breathing rates ($F_{8,280} = 6.18$, Geiser-Greenhouse $\epsilon = 0.5244$, adjusted $P < 0.001$). The effect of metronome-guided breathing rate on HF power tended be smaller in patients with heart disease than in healthy subjects, although the interaction between the presence of heart disease and metronome-guided breathing rate was not significant ($F_{8,280} = 1.87$, adjusted $P = 0.12$). Whereas the decrease in HF power due to changes in the rate of breathing was statistically significant, it was quite small. The average decrease in HF power was only 9.9% from baseline

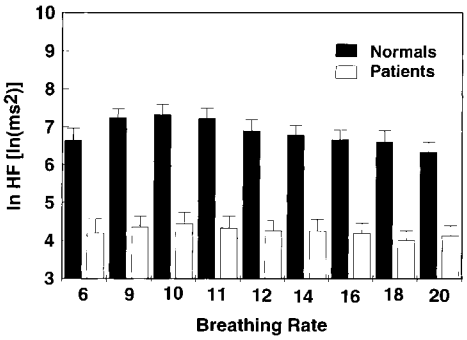

Fig. 5. Comparison of mean values for the logarithm of HF power measured while healthy subjects and cardiac patients were breathing cued to a metronome at different breathing rates. HF power was measured in all subjects at all metronome-guided breathing rates. There is a slight drop in HF power at higher breathing rates that is small compared with the large differences in HF power between healthy subjects and cardiac patients.

and occurred more or less steadily from 9 to 20 breaths/min.

Given this slight but significant tendency for HF power to decrease with increasing metronome-guided breathing rates, we evaluated whether this decrease in HF power was related to the subject's spontaneous breathing rate. We hypothesized that subjects with lower spontaneous breathing rates may have been more uncomfortable breathing at the higher metronome-guided breathing rates, which may have accounted for the reduction in HF power. To evaluate this possibility, we regressed HF power measured at each metronome-guided breathing rate against that rate for each subject. The average slope (HF power vs. metronome-guided breathing rate) for the 39 subjects was -0.0578 ± 0.0750 (SD). This small decrease in HF power with increasing metronome-guided breathing rates was only weakly related to the subject's baseline spontaneous breathing rate ($r = -0.31$).

DISCUSSION

Spontaneous vs. metronome-guided breathing. On the basis of a study in nine normal subjects, it was suggested that the estimation of vagal modulation using RR variability requires control of the rate of breathing (6). Despite this recommendation, most studies have utilized RR variability without regulation of breathing rate. The purpose of this study was to compare the estimation of vagal modulation during spontaneous and metronome-guided breathing. Our data demonstrate that there is no significant difference in HF power measured during spontaneous and metronome-guided breathing at the same rate. In addition, the magnitude of any possible difference in HF power between spontaneous and metronome-guided breathing is much less than the differences in HF power between healthy subjects and patients with cardiac disease. Our data agree with those of Hayano et al. (10), who also demonstrated in a small study of normal subjects that there was no difference between HF power measured during spontaneous and metronome-guided breathing at the same rate.

Whereas the differences between HF power during spontaneous and metronome-guided breathing were small and not statistically significant, we did notice a trend toward increased HF power during metronome-guided breathing. It has been previously shown that increased depth of breathing, or tidal volume, is associated with a small increase in HF power (6). Among our subjects, the tidal volume associated with metronome-guided breathing tended to be larger than the tidal volume associated with spontaneous breathing (Fig. 4), although we did not quantify tidal volume.

Pagani et al. (12) reported differences in the measurement of HF power (using normalized units) during spontaneous and metronome-guided breathing. The measurement of HF power used by Pagani et al. utilizes the amplitude of the peak HF component of the power spectrum, which is different from measurement

American Journal of Physiology – Heart and Circulatory Physiology

Downloaded from ajpheart.physiology.org on November 5, 2005

of HF power used in this study, which used the area under the power spectral density curve between 0.15 and 0.40 Hz. The measurement of HF power utilizing the amplitude of the peak of the HF component is extremely dependent on the shape of the power spectrum. This is extremely important in the context of this study, because the shape of the power spectrum is dependent on variability in the rate of breathing. Variability in rate of spontaneous breathing is reflected in a lower-amplitude and broader peak at the mean respiratory frequency. In other words, RR variability is "spread out" over a range of respiratory frequencies. During metronome-guided breathing, the precisely regular respiratory oscillations are reflected by a single high-amplitude peak in the spectrum with a narrow base. With this in mind, a comparison of HF power during metronome-guided and spontaneous breathing using a measurement of HF power that utilizes the peak of the HF component would be much less reliable than a measurement of HF power that is based on the area under the power spectral density curve.

Effect of increasing breathing rate on HF power. The relationship between increasing breathing rate and HF power during metronome-guided breathing revealed a trend toward a small decrease in HF power with increasing breathing rate. This trend was more pronounced in the healthy subjects than in the patients with cardiac disease. An inverse relationship between breathing rate and HF power has been previously reported (6, 7, 10, 11). However, within the range of normal breathing frequencies (9–20 breaths/min), the magnitude of the effect is small. In this study, HF power fell by ~0.5 log units through the range of normal breathing rates, an extremely small effect compared with the large difference (~2.5–3 log units) between cardiac patients and healthy subjects. These data suggest that correcting HF power for breathing rate is unnecessary. In addition, a consensus paper written by an international group of experts on the use of RR variability did not suggest such a correction (16). Further studies are needed to examine the use of RR variability as a measure of vagal modulation in subjects with breathing rates outside the physiological range.

The recommendation that the rate of breathing must be controlled to estimate vagal modulation was made by Brown et al. (6) using a measurement of RR variability referred to as "respiratory frequency R-R interval power." In this small study, nine healthy subjects were asked to breathe at seven frequencies from 6 to 24 breaths/min. Brown et al. measured respiratory frequency R-R interval power as the area under the peak at the measured breathing frequency at the subjects' breathing rate rather than within the fixed frequency bandwidths used in this and many other studies (HF power = 0.15–0.40 Hz). Respiratory frequency R-R interval power appeared to vary significantly at different breathing frequencies, and the authors concluded that the rate of breathing must be controlled if RR variability is to be used to estimate vagal modulation.

There are a number of important problems, however, with the study by Brown et al. (6) and its interpretation. First, there is no comparison with spontaneous breathing: all data were collected during metronome-guided breathing. Second, the differences in respiratory frequency R-R interval power at different breathing rates occurred primarily because of a 10-fold increase in respiratory frequency R-R interval power at a breathing rate of 6 breaths/min (corresponding to a frequency of 0.10 Hz). Estimation of vagal modulation from RR variability from a subject breathing at 6 breaths/min (0.1 Hz) is problematic, because at this frequency, R-R intervals are modulated by the parasympathetic nervous system (at the ventilatory frequency of 0.1 Hz) and by the sympathetic nervous system (at the Mayer wave frequency of 0.1 Hz). In trying to estimate vagal modulation in a subject breathing at 6 breaths/min, the problem that occurs with the measurement used by Brown et al., the respiratory frequency R-R interval power, is that the measurement includes sympathetic and parasympathetic influences on the sinus node. It is not surprising that RR variability measured at the subject's breathing rate (as is done by Brown et al.) would be markedly reduced when a subject's breathing rate is increased from 6 to 12 breaths/min, since the measurement at 6 breaths/min includes the influence of the sympathetic nervous system on RR variability and the measurement at 12 breaths/min does not include these sympathetic influences.

Besides being cumbersome, metronome-guided breathing has other problems that complicate the interpretation of HF power. The proponents of metronome-guided breathing to measure vagal modulation base their recommendation on the potential problem of comparing HF power between different individuals with different breathing rates. However, in our data, the association between spontaneous breathing rate and HF power measured during spontaneous breathing was relatively weak ($r = -0.32$ and -0.42 for healthy subjects and patients with heart disease, respectively), suggesting that breathing rate by itself is not an important determinant of HF power. In addition, the intervention of metronome-guided breathing introduces other biases into the measurement. Breathing to a metronome requires a certain amount of mental concentration that tends to decrease HF power (15). Metronome-guided breathing also tends to be deeper (i.e., larger tidal volumes), which has also been shown to affect autonomic balance and increase HF power (6). Finally, De Meersman et al. (7) demonstrated convincingly that interventions that control and modify breathing rate and tidal volume are associated with significant levels of subject discomfort and a reduction in HF power. Although our data suggest that the sum of these effects is small, these various effects of metronome-guided breathing add error to the estimation of vagal modulation using RR variability.

Potential mechanisms. The small decrease in HF power with increasing breathing rates may reflect true

American Journal of Physiology – Heart and Circulatory Physiology

Downloaded from ajpheart.physiology.org on November 5, 2005

changes in autonomic modulation. However, several reports suggest that sinus node behavior may be influenced by ventilatory-mediated effects that do not involve changes in sympathetic and parasympathetic nerve firing. Hayano et al. (10) studied seven healthy male medical students in the setting of β-adrenergic blockade and found that as the rate of metronome-controlled breathing increased from 0.10 to 0.33 Hz, HF power decreased while mean R-R intervals remained the same. This finding suggests that the effects of increased breathing rates may produce changes in the power spectral components that do not necessarily reflect alterations in cardiac parasympathetic modulation. Further evidence for changes in RR variability that do not involve changes in autonomic nerve activity has been found in patients after heart transplants. In denervated hearts where there are no vagal influences in RR variability, small oscillations in R-R intervals are observed at breathing frequencies (3).

The mechanism of this type of effect of breathing on RR variability is poorly understood. Saul et al. (14) suggested that there are mechanical changes in the thorax associated with breathing that may result in mild stretching of the sinus node, which may in turn alter its properties in firing behavior. Eckberg (8) suggested, on theoretical considerations, that the kinetics of the sinus node responses to ACh may be different during increased breathing rates when ACh released during expiration may not have time to be completely expressed before the next breath, resulting in an attenuated change in R-R intervals. Importantly, although the existence of this type of ventilatory-mediated modulation of R-R intervals that is independent of autonomic nervous activity is an interesting phenomenon, the magnitude of this effect is extremely small.

Conclusion. HF power during spontaneous breathing and that during metronome-guided breathing are significantly different at the same breathing rates. In addition, HF power is relatively constant across the range of typical breathing rates. The relatively small decline in HF power at higher breathing rates is 2 log units less than the large discrepancies observed between healthy subjects and many samples of patients with cardiovascular disorders. As discussed above, our data indicate that there is no need to control breathing rate to interpret HF power when RR variability (and specifically HF power) is used to identify high-risk cardiac patients.

This research was supported in part by National Heart, Lung, and Blood Institute Grant HL-03466 and was conducted in the Irving Center for Clinical Research supported by National Institutes of Health Grant 5 M01 RR-00645.

REFERENCES

1. **Akselrod S, Gordon D, Ubel FA, Shannon DC, Barger AC, and Cohen RJ.** Power spectrum analysis of heart rate fluctuations: a quantitative probe of beat-to-beat cardiovascular control. *Science* 213: 220–222, 1981.
2. **Berger RD, Akselrod S, Gordon D, and Cohen RJ.** An efficient algorithm for spectral analysis of heart rate variability. *IEEE Trans Biomed Eng* 9: 900–904, 1986.
3. **Bernardi L, Keller F, Sanders M, Reddy PS, Griffith B, Meno F, and Pinsky MR.** Respiratory sinus arrhythmia in the denervated human heart. *J Appl Physiol* 67: 1447–1455, 1989.
4. **Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Schneider WJ, and Stein PK.** RR variability in healthy, middle-aged persons compared with patients with chronic coronary heart disease or recent acute myocardial infarction. *Circulation* 91: 1936–1943, 1995.
5. **Bigger JT Jr, La Rovere MT, Steinman RC, Fleiss JL, Rottman JN, Rolnitzky LM, and Schwartz PJ.** Comparison of baroreflex sensitivity and heart period variability after myocardial infarction. *J Am Coll Cardiol* 14: 1511–1518, 1989.
6. **Brown RB, Beightol LA, Koh J, and Eckberg DL.** Important influence of respiration on human R-R interval power spectra is largely ignored. *J Appl Physiol* 75: 2310–2317, 1993.
7. **De Meersman RE, Reisman SS, Daum M, Zorowitz R, Leifer M, and Findley T.** Influence of respiration on metabolic, hemodynamic, psychometric, and R-R interval power spectral parameters. *Am J Physiol Heart Circ Physiol* 269: H1437–H1440, 1995.
8. **Eckberg DL.** Sympathovagal balance: a critical appraisal. *Circulation* 96: 3224–3232, 1997.
9. **Fleiss JL.** *Design and Analysis of Clinical Experiments.* New York: Wiley, 1986, p. 227.
10. **Hayano J, Mukai S, Sakakibara M, Okada A, Takata K, and Fujinami T.** Effects of respiratory interval on vagal modulation of heart rate. *Am J Physiol Heart Circ Physiol* 267: H33–H40, 1994.
11. **Hirsch JA and Bishop B.** Respiratory sinus arrhythmia in humans: how breathing pattern modulates heart rate. *Am J Physiol Heart Circ Physiol* 241: H620–H629, 1981.
12. **Pagani M, Lombardi F, and Guzzetti S.** Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. *Circ Res* 59: 178–193, 1986.
13. **Pomeranz B, Macaulay RJB, Caudill MA, Kutz I, Adam D, Gordon D, Kilborn KM, Barger AC, Shannon DC, Cohen RJ, and Benson H.** Assessment of autonomic function in humans by heart rate spectral analysis. *Am J Physiol Heart Circ Physiol* 248: H151–H153, 1985.
14. **Saul JP, Berger RD, Albrecht P, Stein SP, Chen MH, and Cohen RJ.** Transfer function analysis of the circulation: unique insights into cardiovascular regulation. *Am J Physiol Heart Circ Physiol* 261: H1231–H1245, 1991.
15. **Sloan RP, Korten JB, and Myers MM.** Components of heart rate reactivity during mental arithmetic with and without speaking. *Physiol Behav* 50: 1039–1045, 1991.
16. **Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.** Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation* 93: 1043–1065, 1996.

American Journal of Physiology – Heart and Circulatory Physiology

Downloaded from ajpheart.physiology.org on November 5, 2005