

WINDOWS BASED PACKAGE FOR HEART RATE VARIABILITY ANALYSIS

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Abstract--- Heart rate variability reflects the haemodynamic interplay between perturbations to cardiovascular function and the dynamic response of the cardiovascular regulatory systems. Modern signal processing techniques provide a means of analysing beat to beat fluctuations in cardiovascular signals, so as to permit a quantitative, noninvasive method of assessing closed loop haemodynamic regulation and cardiac electrical stability. This method promises to provide a new approach to the clinical diagnosis and management of disorders of cardiovascular regulation and stability. We have developed and tested a package that performs HRV analysis according to the Internationally suggested standards. Some of the National Institutions are already using it for their clinical research work on a regular basis.

Index terms--- heart rate variability, autonomic balance,

1 INTRODUCTION

The heart rate variability (HRV) signal derives its significance from the facts that (i) it provides a noninvasive window to study the autonomic nervous system (ANS), (ii) it is altered in different disease states and (iii) changes in ANS activity may be important indicators of patient outcome. A healthy heart does not beat at a regular, constant rate. In fact, one can almost say that perfectly rhythmic activity occurs only in disease. Some of the factors which affect HR are breathing [1], posture [2], physical activity [3], mental stress [4], different stages of sleep and circadian rhythm [5]. The determinants of the respiratory fluctuations in heart rate include a stretch reflex from the lungs and thoracic wall, changes in cardiac filling, arterial baroreceptor responses to blood pressure changes, changes in baroreflex sensitivity with respiratory phase, and respiratory center activity overflow to medullary vasomotor neurons [6]. The pattern of these changes are modified in pathological conditions such as post myocardial infarction, diabetes and psychiatric disorders such as alcoholism and depression. HRV analysis concerns with the systematic,

quantitative study of the fluctuations in the heart rate. The time and frequency domain parameters that are usually measured from this HRV signal are indirect indicators of the integrity of the control mechanisms that cause the variability. Thus, the HRV investigations provide a useful non-invasive window to measure neurocardiac control.

In this paper, we present our work on developing a standard package for performing HRV analysis in strict accordance with Internationally suggested standards. This can be very advantageously used by any research group working on any aspect related to sympathetic and parasympathetic imbalance in the autonomic system.

2 METHOD

A noise-free record of ECG is obtained lasting several minutes. For short-time analysis, a record of 5 minutes duration is suggested. For long-time analysis, 24-hour recordings are recommended, and in any case, not less than 18 hours of analyzable ECG data that includes the whole night. In certain studies, ECG is recorded twice from the subject, first in supine position and then, immediately after standing (or tilt). This enables one to study the changes, mediated through the baroreceptors, resulting from the orthostatic stress. The ECG is sampled at a sufficiently high rate (usually 500 Hz) to determine the time locations of the R waves at the accuracies needed for the analysis.

The R waves are detected using a suitable algorithm [15], and the so-called normal-to-normal (NN) intervals (that is, all intervals between adjacent QRS complexes resulting from sinus node depolarizations) are determined. From this R-R interval series, several time domain descriptors of the variability are computed. Alternatively, the instantaneous heart rate series is first obtained from the R-R intervals Fig. 1 shows a typical HR time series plotted against the time of occurrence of the R waves, with the subject in supine position. Fig. 2 shows the HR values obtained for the same subject immediately after standing. The sudden increase in HR due to orthostatic stress is clearly seen. The HR signals shown in Figs. 1 and 2 are discrete-time signals, with unequal time intervals (corresponding to individual R-R intervals) between the individual values. This data is suitably interpolated [7] to

obtain evenly spaced (in time, usually 0.25 sec) heart rate samples. From this time series, the mean is removed to obtain the Heart Rate Variability point series. Various spectral parameters are then computed from this signal.

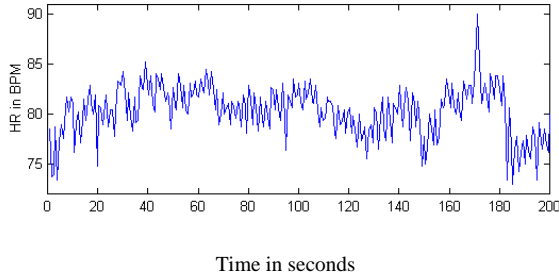


Fig. 1. A typical HR Time Series with the subject in supine position.

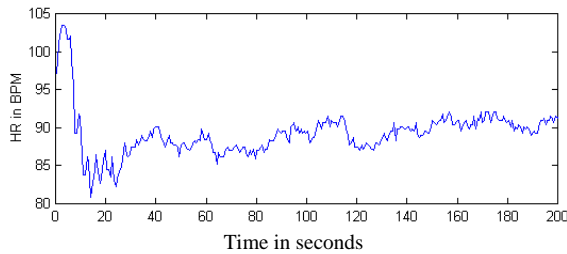


Fig. 2. HR Time Series immediately after the subject stood.

(a) Time Domain Analysis

From the original R-R intervals, a number of parameters are calculated: MRI, the mean R-R interval, SDANN, the standard deviation of the mean R-R intervals of consecutive short periods, SDNN, the standard deviation of the NN intervals, MAD, the mean of the absolute differences between consecutive R-R intervals, RMSSD, the root mean square successive difference of intervals, pNN50, the number of successive RR intervals which differ by more than 50 msec expressed as a percentage of the total number of ECG cycles analyzed, E/I, the ratio, as well as E-I, the difference between the maximum (E) and minimum (I) heart periods (E and I typically occur during some Expiratory and Inspiratory phases respectively of the breathing cycle). Also computed is the Coefficient of Variation, $CV_{R,R}$, defined as the ratio of the standard deviation of the R-R intervals to their average value. The HRV triangular index is the integral of the density distribution divided by the maximum of the density distribution. Using a measurement of NN intervals on a discrete scale, the measure is approximated by the value (total number of NN intervals)/(number of NN intervals in the modal bin), which is dependent on the length of the bin, that is, on the precision of the discrete scale of

measurement. Of the above, the four standard measures are SDNN, SDANN, RMSSD and HRV triangular index.

(b) Spectral Domain Analysis

In order to obtain the power spectrum, we need to have uniform time-interval samples of either the HR, or the R-R intervals. Since HR values are available only at the R occurrence instants, we need some interpolation technique. The usual value of (re)sampling frequency used for the HR signal is 4 Hz. The criterion for selecting the resampling frequency is that the Berger's algorithm [7] is accepted as one of the standard techniques in the literature. Here, to find out the interpolated HR value at any specific time instant, a time window of twice the sampling interval (in this case, 0.5 sec) is considered centered around the instant of interest. The no. of R-R intervals (n) that fall within this local window is divided by the width of the window to arrive at the interpolated HR value. n is arrived at as follows. Suppose t_1 sec. of the window lies in the R-R interval P_{n-1} , and the remaining t_2 sec. ($t_1+t_2 = 2T_s$) lies in P_n . If T_{n-1} and T_n are the corresponding R-R intervals, the $n = t_1/T_{n-1} + t_2/T_n$. However, in the author's experience, a simple linear interpolation gives results as good. From this uniform interval HR series, the mean is then removed. Either non-parametric (FFT) or parametric (usually, Autoregressive) spectrum of this HRV signal is then obtained. Fig. 3 shows sample HRV spectra for supine and standing postures of a subject. By means of studies where the autonomic components were selectively blocked, they have identified that different frequency components in the HRV spectrum have been contributed by different aspects of the physiological system. Based on the results of these studies, the spectrum is divided into three distinct bands, namely, the very low frequency band (VLF, frequency range 0.01-0.04 Hz), the low frequency band (LF, 0.04 - 0.15 Hz) and high frequency band (HF, 0.15-0.40 Hz). Drugs such as atropine are selective parasympathetic blocking agents and by employing them on normal individuals, the HF peak has been identified to be correlated to the respiratory driven vagal (parasympathetic) efferent input to the sinus node. Similarly, propranolol is a strong sympathetic receptor blocker, with the help of which, the LF band (definitely during standing position) has been known to be caused by the sympathetic vagal drive. The VLF band is supposed to be linked to the thermoregulatory system, though the evidences are inconclusive. Accordingly, the absolute power (in millisecond squared) in all the 3 frequency bands and ratios of HF and LF to total HRV power are calculated. A ratio of the energies in the LF and HF bands is currently being accepted as representing sympathovagal balance. LF norm and HF norm are the LF and HF powers in normalized units (ie. LF or HF/(total power-VLF) * 100, where total power is defined as the power in the

frequency band ≤ 0.4 Hz. The representation of LF and HF in normalized units emphasizes the controlled and balanced behaviour of the two branches of the ANS and also tends to minimize the effect of the changes in total power on the values of LF and HF components.

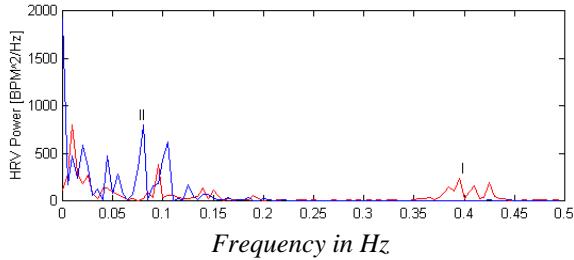


Fig. 3. Power Spectrum of HRV (I - Supine; II Standing)

Though most studies have analyzed the HRV samples, a few investigators [Murata] have directly obtained the power spectrum of the R-R interval series, ignoring the fact that the latter is a non-uniformly sampled data. These results are not always directly comparable to those obtained from the HRV series. An article by Castiglioni [9] discusses in detail the advantages, disadvantages and the relationship between these two methods of analysis. It is now suggested that properly interpolated RR interval tachogram be used with the nonparametric method. Another problem in comparing results of different groups using parametric spectrum is that the model order is rarely specified. Snapshots of the filtered ECG data and the displayed HRV spectra are shown in Figs. 4 and 5, respectively.

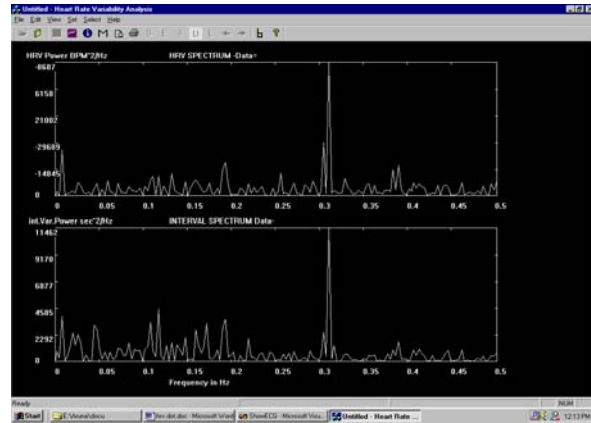


Fig. 5. HRV Power Spectra.

3 CLINICAL APPLICATIONS

The anatomic location of the autonomic nervous system (ANS) renders it inaccessible to direct physiological testing. The study of HRV Power Spectra is gaining acceptance as a non-invasive method for identifying the role of the ANS in regulating cardiac function. HRV decreases with age and this factor must be kept in mind while interpreting the results of any study. It may be possible to roughly normalize the data with respect to age. HRV analysis being a field of current research, the possible clinical applications are increasing. The following are some of the potential clinical uses already identified.

Risk Stratification of Post Myocardial Infarction Patients

Decreased heart rate variability is a strong and independent predictor of adverse outcome after acute myocardial infarction (MI). Either time or frequency domain measures are excellent predictors of death or arrhythmic events after MI and they are equivalent for this purpose. Post-infarction patients with low HRV exhibit a profound autonomic imbalance that results in an increased incidence of sudden death [9]. The presumed pathologic mechanism for the sudden death is the excessive autonomic discharge, especially norepinephrine and epinephrine. The relative risk of patients with a R-R interval variance of $<1000 \text{ msec}^2$ has been found to be 3.8. HRV index is equivalent to left ventricular ejection fraction (LVEF) for predicting all-cause mortality, but is better than LVEF or Signal Averaged ECG for predicting arrhythmic events. Similarly, power spectral analysis of HRV could also be used to categorize patients according to risk of sudden cardiac death.

Psychiatry

The significance of HRV analysis in psychiatric disorders arises from the fact that one can easily detect a sympatho-vagal imbalance (relative cholinergic and adrenergic modulation of HRV), if it exists in such

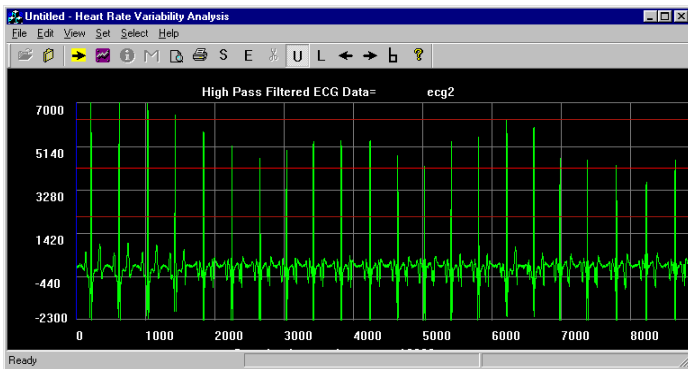


Fig. 4. High Pass Filtered ECG data

pathologies. It has also been applied to identify possible autonomic dysfunction resulting from the side effects of pharmacological treatment. In situations such as this, one needs to eliminate subjects known to have cardiovascular diseases.

HRV Analysis of Holter Data

The power in the very low frequency (VLF) band (from DC to about 0.03 Hz) of the HRV spectrum is probably due to slow mechanisms of regulation such as humoral and thermoregulatory factors. Obtaining a single power spectrum over a long period can help investigate the long term regulatory mechanisms involved in the VLF component. However, the sampling frequency in current Holter systems is 125 Hz, thus limiting the resolution of measurement of R-R intervals. The interpretation of results is also obscured by the fact that the patient's dynamic state keeps varying during the recording.

Sleep Research

To study the autonomic mechanisms in sleep, HRV may serve as one of the techniques. HR is significantly reduced during all stages of non_REM sleep. Normal healthy individuals studied during sleep using the above techniques show an elevated vagal modulation during stages 1, 2, 3, and 4, whereas REM sleep is characterized by decreased respiratory sinus arrhythmia (i.e., reduced HF power in HRV spectrum).

Heart Transplantation

Following transplantation, the heart rhythm is completely controlled by the donor sinoatrial node with no neurally mediated influence from the recipient. The power spectra of HRV of such a donor organ, devoid of autonomic innervation, has been observed to resemble a white noise power spectrum. However, in only one isolated case, all parameters of HRV were indistinguishable from normal subjects, including responses to respiration, orthostatic stress, etc. [10]. This suggests possible functional reinnervation in the human heart allograft. Thus, HRV analysis offers a unique method of establishing reinnervation of human transplanted hearts.

Yoga Research

Since yogasanas, pranayama and meditation bring about autonomic balance by acting on the neuroendocrine system, testing the status of the Autonomic Nervous System (ANS) of an individual could prove to be a very useful exercise in understanding and validating of the effects produced by any one or more of the above practices. In postures such as *savasana* and certain types of meditation, one can expect possible accentuation of parasympathetic activity. On the other hand, with the *kriya* techniques, at least during the practice, one can probably look for sympathetic dominance. In forced nostril breathing techniques, (such as

Suryanuloma and *Chandranuloma*), one would hope to see selective increase in sympathetic or parasympathetic activity. But, after a prolonged practice of a comprehensive set of yogasanas, the author expects to see a better integration of the body's autonomic function, independent of the initial direction of imbalance. This, if demonstrated, would prove to be an invaluable piece of evidence in favour of yoga as against pharmacological intervention.

Other Applications

This provides another sensitive non-invasive method of detecting autonomic neuropathy in diabetes. Spectral studies in diabetics have shown lower LF/HF ratio during tilting as compared to normal subjects, whereas no significant difference was observed in supine state. In addition to the above mentioned applications, changes due to exercise, relation between autonomic cardiac function and the clinical and angiographic features of myocardial ischemia and autonomic imbalance in patients with congestive heart failure [11] have been studied exploiting the advantages of the above techniques. HRV analysis might prove to be a valuable tool in the study of exercise mediated autonomic changes.

4 CONCLUSION

This software has evolved over time based on the feedback and inputs from a number of research groups in leading organizations, namely, Dr. W.Selvamurthy, Director, Defence Inst. of Physiology & Allied Sciences, Delhi, (ii) Dr. B. N. Gangadhar, Additional Professor, Dept of Psychiatry, NIMHANS, Bangalore, (iii) Dr.A.S.Arvind, Institute for Aerospace Medicine, Bangalore, and (iv) Dr.Shirley Teles, Asst. Director of Research, Swami Vivekananda Yoga Research Foundation. Modifications were also incorporated when the International standards [] were proposed. A number of software features have been upgraded recently from the point of view of user-friendly controls.

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