A Study of Respiratory Modulation of Cardiac Inter Beat Interval

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A study has been made to establish the complex relationship between the changes in the rate of breathing and subsequent modulation of cardiac interbeat intervals. Spectral analysis and the system function studies in complex frequency domain were effectively used with the help of Digital Computer to arrive at quantifiable results. Some basic assumptions have been shown to be erroneous and steps required to avoid these pitfalls have been highlighted. The study showed the possibility of correctly predicting certain change in the cardiac interbeat interval pattern under different breathing conditions.

Introduction

Modulation of the heart rate due to respiration has been observed and studied since many years. Periodic electro-physiological and mechanical activity of the heart is initiated by the sinus node and the modulation of the sinus rhythm is called sinus arrhythmia where cardio-acceleration is associated with inspiration and cardiac slowing with expiration. However, on closer studies this basic assumption has not been found to be entirely correct and thus an effort has been made to establish the complex inter-relationship by using spectral analysis and system function study with the help of Digital Computer.

There are two central problems in this study—requirement of a satisfactory, detailed, quantitative representation of the beat-by-beat variations of the heart which can be explored in respect of its potential relation to other physiological time-varying processes; and the need for a correct analytical technique whereby a definite relation can be established and preferably quantified. Though the existence of a relation between respiration and variations in the heart rate has been commonly observed and studied, quantitative analysis of the relation has been rather scanty. A generalised statement describing sinus arrhythmia to be 'in phase' with breathing and thence deducing a cause-and-effect relation between different systems is incomplete which also gives an idea of a similar response irrespective of the variations in respiration. The success in establishing a quantifiable relation between these two parameters would, therefore, help in correctly predicting the change in heart rate in association with any type of breathing in normal and physiologically abnormal conditions like hypoxia, pressure breathing, hyperventilation, etc. This is

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likely to help in explaining some of the ECG variations among normal individuals leading to a better evaluation.

The rate of breathing over a given time interval should provide much information about the corresponding heart rate fluctuations around the mean value. However, it has been found that respiratory variations of the heart rate is a phenomenon

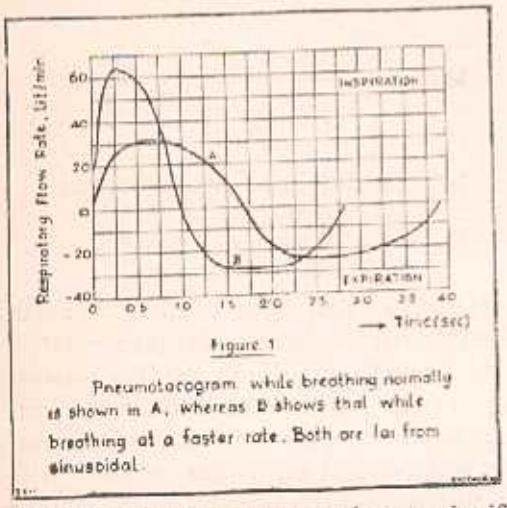


Figure 1

Pneumotacogram while breathing normally as shown in A, whereas B shows that while breathing at a faster rate. Both are far from sinusoidal.

where breathing frequency takes a significant part and thus an attempt can be made to describe the system response with its specific characteristics. The apparent pitfall in this type of experiment has to be kept in mind. An attempted constant rate of breathing by the subject is usually expected to be of sinusoidal pattern and is considered to have a single frequency per unit time. Recorded respiration from a pneumotachograph in Fig. 1, can explain the basic erroneous assumption of a single frequency content of the respiration signal. It can be seen that this type of signal can hardly be called as a sinusoidal waveform of one frequency and the system response calculated on this assumption cannot be true except in a very gross way. Fourier analysis is of great value in analysing such a signal.

Mathematical Basis

A time-varying signal f (t) can be represented by a Fourier series consisting a range of frequencies, each of which is represented by a sine and a cosine term and thus represented as :

$$f(t) = \tfrac{1}{2} a_0 + \sum_{n=1}^{\infty} (a_n \ Cos\, n\omega_0 t + b_n \, Sin\, n\omega_0 t)$$

and in complex plan

$$f(t) = \tfrac{1}{2} a_0 + \sum_{n=1}^{\infty} Cn. \, Cos\,(n\omega_0 t + \phi_n)$$

where

$$Cn = \sqrt{a_n^2 + b_n^2}, \quad \phi_n = arctan\,(b_n / a_n)$$

While analysing the variations in the heart rate the nature of the fluctuation over a period of time cannot be truly represented by the mean value or the short-term variations of the mean or of the standard deviation. A better way of dealing with this problem is to study the sequence of intervals between successive heart beats, i.e. the cardiac interbeat interval, which carries information about beat-by-beat variations. The cardiac interbeat interval sequence thus obtained, can then be treated as interval signal and this greatly enhances the investigating capabilities because highly powerful modern techniques of signal analysis can then be employed.

Analysis of a linear system can then be achieved with a given input in the form of breathing and observing the output in the form of cardiac interbeat interval as in Figure 2.

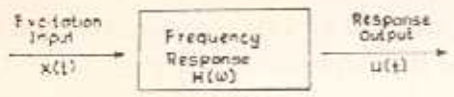


Figure 2

A schematic representation of a system response with a given input and observed output

Consider x(t) as an input to and u(t) as an output from the system whose impulse response, expressed in the complex frequency domain, is $H(\omega)$. The frequency response can be calculated by a complex frequency technique as follows. If we get the transform of x(t) as $X(\omega)$ and of u(t) as $U(\omega)$, provided $X(\omega)$ contains all relevant frequencies, then the frequency response, $H(\omega)$ is given by

$$U(\omega) = u + jv$$
$$X(\omega) = x + jy$$
$$\text{and } H(\omega) = \frac{u + jv}{x + jy}$$

These are in complex frequency domain, each component representing both real and imaginary parts, which may be solved and written as

$$H(\omega) = \frac{ux + vy}{x^2 + y^2} + \frac{j\ vx - uy}{x^2 + y^2}$$

and in general term be represented as

$$H(\omega) = R(\omega) + j\,S(\omega)$$

The term frequency content is worth clarifying at this stage. Frequency refers to be fluctuations of the cardiac interval signal from a mean value and not the instantaneous heart rate values. With a constant heart rate of say 60 per minute, with no fluctuations the energy content will be localised at zero frequency having a d.c. or constant value only. Fluctuations from this constant will lead to nonzero frequency values.

The process of finding the frequency response of a system requires the division of the interval spectrum by the respiration spectrum at each frequency in the complex domain, thus determining the frequency response to an input signal of uniform spectrum. However, in case of those frequencies for which respiratory components are small, a significant contribution due to noise will be present. For this reason, a technique has to be devised in order to ensure that all spectral components of the

Figure 3

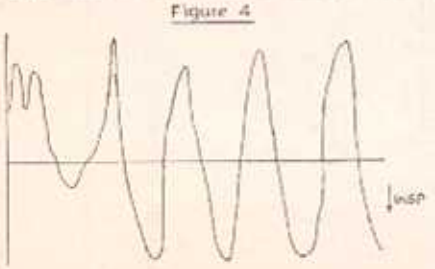
Block diagram showing recording and analytical sequence in computer study.

equivalent input signal were of respiratory origin.

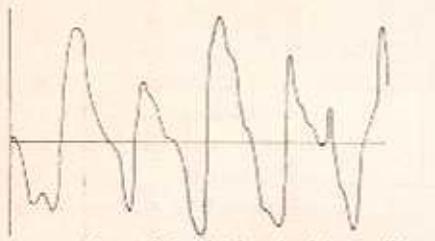
Method and Findings

A block diagram showing the method is given in Figure 3. E C G was recorded continuously in orthogonal lead system simultaneously on 3 channels of a multichannel Tape Recorder in FM mode on analog tape. Respiratory movement was also recorded on the fourth channel through a Respiration Monitor using suitable transducer. Analog-Digital conversion was done by IBM 1800 computer at the rate of 400 samples per second per channel. Quality of data was checked and displayed by suitable programs. High frequency electronic and tape noise were removed by digital filtering. These are physically non-realisable filters but can be mathematically achieved to obtain a very high precision. Computer programs were made for automatic identification of the

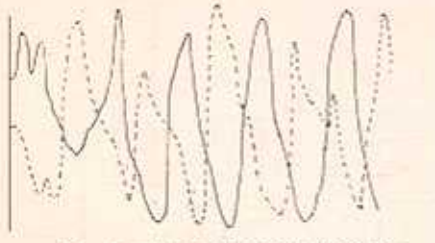
Figure 4



Respiration at 3 breaths per minute sampled during 128 cardiac intervals.

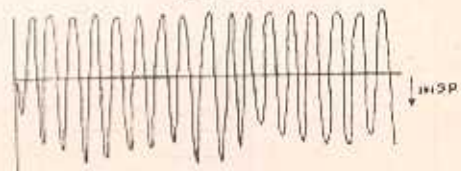


Cardiac interbeat interval while breathing at the rate of 3 per minute.

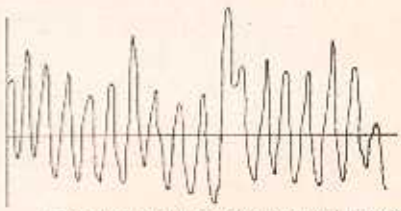


Two signals superimposed where the cardiac interval is shown in dotted line.

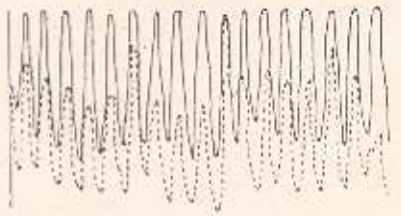
Figure 5



Respiration at 12 breaths per minute sampled during 128 cardiac intervals



Cardiac interbeat interval while breathing at the rate of 12 per minute.



Two signals superimposed where the cardiac interval is shown in dotted line.

R-peaks, the previous T-P intervals and the beginning of the P waves using a spatial velocity method. This method helps in identifying the minimum electrical activity in 3-dimensional space in atrial tissue. From these, P-P intervals were computed and the sequence was stored in the computer memory and later transformed to Data cards and Magnetic tape for further analysis. Corresponding respiration signal samples were also identified enabling to coincide with the equal-interval cardiac interval samples. This procedure also facilitated Fourier analysis by using Fast Fourier Transform[4] in processing fixed length data samples. Figure 4 and 5 show two sets of data at different breathing rates. The change in the pattern of interval fluctuations can be noted. More interesting is the change in phase difference which is very apparent in these figures. Spectral analysis of respiration and corresponding interval signals were done by the Fast Fourier Transform. A number of experiments were conducted with each subject breathing at different rates to obtain a set of recording. The spectral analysis of each breathing signal thus obtained, shows a spectral band of moderate activity instead of a single frequency, with the band depending on the basic rate of breathing. From each set of data the frequency response of the system over the band-limited spectrum was calculated and stored and ultimately the total system response was obtained. The analysis was conducted on a number of normal subjects and the amplitude spectra was found to be remarkably similar. This is shown in Figure 6. With the system response thus obtained, the subjects were told to undertake different specific types of breathing while simultaneously recording the interval and respiration signal. The actual variation of cardiac interbeat interval with the calculated expectation were compared which are found to be highly comparative.

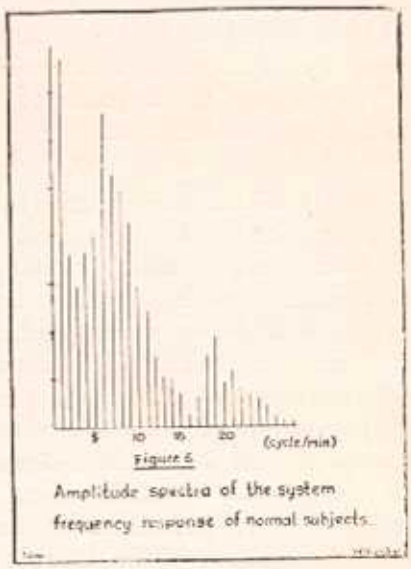


Figure 6

Amplitude spectra of the system frequency response of normal subjects

Discussion

Respiration plays an important part in the variations of ECG in normal subjects by altering the rate, rhythm, as well as the morphological pattern. Many investigators have studied to establish the modes of action of respiration in modulating the heart rate. Anrep and co-workers[3] observed that respiratory sinus arrhythmia was caused by simultaneous action of direct pulmonary reflex and the central medullary action. Hering-Breuer reflex provides a regulatory feed back where inflation of the lungs tends to terminate inspiration and deflation of the lungs tends to initiate it. Manzotti[5] observed that the respiration alters blood flow as well as blood pressure. The concomittent modu-

lation of the baro-receptor activity in turn modified the heart rate. During a positive pressure breath holding test, Manzotti[5] observed a gradual increase in the heart rate referable to the slow alteration of circulation, and also that the maximum rise was attained after a time comparable to the time needed to reach a new circulatory equilibrium in response to the magnitude of pressure exerted.

The validity of the Bainbridge reflex, cardio-acceleration with rise in venous pressure due to probable stretching of the atrium and the great veins, have been questioned by many workers. Positive pressure breath-hold should reduce the distention of the right atrium because of lower venous return and thereby should decrease the heart rate, if such reflex exists, instead of accelerating, as observed. Walker and Mackay[8] have shown that the changes in the heart rate accompanying a change in venous return is not due to the action of the receptors in the central veins or right atrium. Heart rate increases only when there is a subsequent rise in the mean arterial pressure. Manzotti suggested that the aortic baroreceptors represent the sensory area of the blood flow heart rate reflex. In experiments of Aviado and co-workers[3] increased pressure in isolated right atrium caused a reflex bradycardia and hypotension. Again, the effect has not been quantified, and it is not known how these receptors interact with aortic and carotid receptors. The Valsalva manoeuvre at normal lung volume (and not after a full inspiration) usually leads to a large rise in the heart rate and this also proves the importance of presso-receptors in effecting a change in heart rate. "Spilling over" of impulses from the respiratory centre to the vasomotor centre during end of inspiration thereby altering blood pressure and heart rate has been proved experimentally. Thus to the present day three mechanisms have been primarily established to explain the phenomenon : (a) a reflex control, directly from the stretch receptors in the lungs and chest; (b) an indirect control through the alteration of blood pressures which again is partly affected by breathing; (c) a central nervous system control by direct communication between the respiratory centre and the vasomotor centre.

The feasibility of extracting and defining the heart rate fluctuations of respiratory origin can lead to a better identification of other physiological causes under different environmental conditions.

It is generally accepted that the response to breathing in heart rate fluctuation is similar in type, namely cardio-acceleration during inspiration and cardiac slowing during expiration. It has been shown that this assumption is not entirely correct and a complex relationship exists which can be effectively calculated and represented as a human system response.

Necessary pitfalls in considering a so-called regular breathing a single frequency function has been highlighted as detailed calculations based on this erroneous assumptions normally would lead to wrong results. From the system response thus deduced a predicted cardiac interval pattern with a given respiration signal is found to be well comparable to the actual signal

recorded. Variations in cardiac rate and rhythm due to respiration can therefore be predicted with reasonable accuracy. The same method may also be effectively used to establish the complex relation with other body systems. This would help in explaining the range of the changes encountered in normal, physiologically abnormal or pathological conditions.

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