The relationship between short-term HRV indices and heart rate response to Deep Breathing Test in normal subjects

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Abstract:
Normally, at rest, respiration is associated with a sinus arrhythmia due to modulation of the cardiac parasympathetic supply. Deep Breathing Test (DBT) thus assesses the parasympathetic arm of nervous system control of the cardiovascular function. Parameters computed from the heart rate responses to the DBT, namely I-EHR and the EI ratio quantifies the extent of sinus arrhythmia and parasympathetic activity. The short-term Heart Rate Variability (HRV) indices that reflect cardiac parasympathetic activity are pNN50, RMSSD, and HF power. The indices that mirror the combined modulation of sympathetic and parasympathetic cardiac supply are SDNN and Total power (sum of LF and HF powers). We postulated that as the DBT was done at a low frequency of breathing (0.1 Hz), changes in the cardiac sympathetic activity would also contribute to the heart rate responses of DBT. The current study thus explored whether there was any correlation between the DBT values of I-EHR and EI ratio and the HRV indices reflecting combined activity of the cardiac sympathetic and parasympathetic innervation, namely SDNN and Total power. We also determined whether there was any correlation between the same DBT values and HRV indices reflecting purely cardiac parasympathetic fluctuations, namely RMSSD, pNN50 and HF power. Towards this, we did the DBT in 22 healthy male volunteers (aged 25-35 years) and their resting supine ECG and respiration was recorded over 5 minutes for short-term HRV analysis to obtain the HRV indices. Spearman's correlation test was applied between the DBT results (I-EHR and EI ratio) and the HRV indices. The results of our study showed no correlation between the DBT parameters and the HRV indices. In conclusion, our study shows that among the subjects studied, the DBT value of a person did not predict the persons HRV indices. Thus, we found no relationship between the inherent spontaneous cardiac autonomic activity and the
Deep Breathing Test values in our subjects. 

**Keyword**: Short-term HRV indices, Deep breathing test, Correlation, Cardiac parasympathetic activity, Cardiac sympathetic modulation

**BACKGROUND:**
Deep Breathing Test (DBT) is a test for assessing the autonomic nervous system control of the cardiovascular function. It evaluates the efferent parasympathetic system supplying the sinoatrial node (1). Normally, at rest, respiration is associated with sinus arrhythmia, that is, an increase in heart rate with inspiration and a decrease during expiration due to variations in the vagal innervation of the SA node of the heart (2–4). This modulation of the cardiac vagal supply is brought about by various reflexes such as the Bainbridge reflex and Baroreflex, involving the stimulation of atrial stretch receptors, pulmonary stretch receptors and arterial baroreceptors. The extent of sinus arrhythmia varies DBT attempts to quantify sinus arrhythmia and is performed by making the patient breathe slowly and deeply at a rate of 6 breaths per min or at 0.1 Hz for one full minute, while the ECG is continuously recorded to calculate the changes in heart rate. From the changes in heart rate, several parameters may be computed to quantify the extent of sinus arrhythmia. Of these, the most commonly computed parameters are the I-EHR and the E/I ratio (6). The I-EHR is the difference between the maximal heart rate during inspiration and the minimum heart rate during expiration, averaged over the 6 cycles. The E/I ratio is the ratio of the longest RR interval during expiration to the smallest RR interval during inspiration, the value being averaged over the 6 cycles. Normal values for these 2 parameters varies with age (7). However a value of I-EHR less than 15 bpm and the E/I ratio of less than 1.21 is considered abnormal, denoting a disorder of the cardiac parasympathetic supply (8), established, which reflect the activity of the two branches of the cardiac autonomic supply. Of these, SDNN (Standard deviation of the Normal-to-Normal RR intervals of the 5 minute ECG) and the sum of LF (Low Frequency) and HF (High Frequency) Power or Total Power reflect the total HRV due to modulation of both the sympathetic and parasympathetic cardiac supply. The RMSSD (Square root of the mean of the sum of the squares of the differences of the successive RR interval), pNN50 (Proportion of the number of pairs of adjacent NN intervals differing by more than 50ms out of the total number of NN intervals in five minutes of ECG) and the HF power reflect the modulation of the vagal supply to the heart (6). Sinus arrhythmia and the parameters of DBT are believed to be purely due to modulation of the parasympathetic supply during inspiration and expiration, based on experimental evidence (2,4). Fluctuations in the cardiac sympathetic supply are not believed to contribute to sinus arrhythmia because of the delay in the response time of the sympathetic system to changing stimuli (inflation and deflation of lungs) at the normal breathing rate. However, there is a school of thought that cardiac sympathetic activity may also influence the extent of Sinus Arrhythmia (9,10). Moreover, while breathing at a slow rate of 6 cycles per min, it can be postulated that the sympathetic supply will also be modulated along with the parasympathetic by respiration. If this were true, there would be a correlation between a person’s inherent spontaneous cardiac autonomic activity and the DBT values. The markers of total spontaneous cardiac autonomic activity are SDNN and Total power.
(LF+HF). On the other hand, if sinus arrhythmia during the DBT is contributed by only the parasympathetic activity, then there would be a correlation between a person’s spontaneous parasympathetic activity and the DBT values. The markers of spontaneous parasympathetic activity are RMSSD, pNN50 and HF power. Hence, the current study sought to explore whether there was any correlation between the results of DBT and the HRV indices reflecting the combined modulation of sympathetic and parasympathetic cardiac supply namely SDNN and Total power (LF+HF powers), in normal subjects. We also explored if there was any correlation between the DBT values and RMSSD, pNN50 and HF power, in normal healthy subjects.

**Objectives:**
The aim of the current study was to investigate if the DBT values namely I-E HR and E/I ratio in normal subjects had any correlation with the resting HRV indices of SDNN, Total power (LF+HF powers), RMSSD, pNN50 and HF power.

**METHODS:**

**Subjects:**
Twenty two healthy male volunteers (aged 30.08 ± 4.4 yrs) without any cardiovascular, respiratory or metabolic diseases were recruited as part of another study being done. All the subjects who were recruited had blood pressures in the normal range and were not on any chronic medications. The study was done in compliance with the Helsinki declaration for experiments with human subjects. The participants were informed of the details of the study and the consent in written form was obtained before the actual experiment. The study was approved by the Institutional Ethics Committee.

**Study protocol:**
The subjects were instructed not to consume any food for at least 2 hours before the time of the test and were instructed to refrain from consumption of caffeinated beverages, alcohol and strenuous physical activity for 24hrs prior to recording. The experiment was done in a quiet, dimly lit room, with an ambient room temperature of 25-26°C in the morning before 11AM. The test instructions were given to the subjects just before the commencement of the test. The subjects were allowed to relax in supine position for 20 min with ECG leads applied in Lead II configuration and the respiratory belt fastened around the chest to monitor and record the heartrate and the respiratory rate respectively, during the rest period. Following the 20min rest period, the ECG and respiration were recorded for another 5min for short-term HRV analysis. Following this, the DBT was performed in the supine position. The subjects were instructed to breathe slowly and deeply at a frequency of 6breaths/min for 1 minute and were guided by verbal commands such that the subject inspired for 5 seconds and expired for 5 seconds. During this time the ECG was continuously recorded. The ECG and respiratory signals were acquired and stored as a digital data in a personal computer using a data acquisition system (BIOPAC Systems, Inc., CA 93117, USA). The sampling rate of 1 KHz was used to acquire the signal.

**DATA ANALYSIS:**
The heart rate (HR) response to DBT was analysed by measuring:

a) **I-E HR:** The lowest heart rate during expiration subtracted from the highest heart rate during inspiration, for each of the 6 cycles and was then averaged.
I-EHR 15bpm was considered normal
b) E/I ratio: The ratio of longest RR interval during expiration and shortest RR interval during inspiration. E/I 1.21 was considered normal.

The 5 min ECG recordings were examined for ectopic beats and noises (6) and the R-R interval was analysed for short-term HRV using Nevrokard aHRV software version 1.1 (Medistar, Slovenia). The Time and Frequency domain short-term HRV indices were analysed. Time domain indices are the output of Statistical tests.

1. SDNN (ms): Standard deviation of the Normal-to-Normal RR intervals of the 5 minute ECG.

2. RMSSD (ms): Square root of the mean of the sum of the squares of the differences of the successive RR intervals.

3. pNN50: Proportion of the number of pairs of adjacent NN intervals differing by more than 50ms out of the total number of NN intervals in five minutes of ECG.

Frequency domain indices are obtained by performing Fast Fourier Transformation (FFT) of the RR interval tachogram, obtained from the 5 minute ECG. The output of the FFT is the power spectrum which gives a graphical distribution of the entire power across different frequencies. By computing the area under the curve over different frequency ranges we get the following indices:

1. 1) HF power: High Frequency Power in ms² in the range of 0.15 – 0.40 Hz. This reflects purely the parasympathetic activity.

2) LF power: Low Frequency Power in ms² in the range of 0.04-0.15Hz. Both sympathetic and parasympathetic modulation of the RR intervals contributes to this power 3) Total power (ms²): LF + HF powers. This represents the total HRV, reflecting activity of both sympathetic and parasympathetic components over 5 minutes of ECG.

**STATISTICAL ANALYSIS:**
The data was found to be not normally distributed. Therefore, the correlation of short-term HRV indices and DBT parameters was done using the non-parametric Spearman’s correlation to obtain Rho (r) value. Analysis was done using SPSS software-version 18.

**RESULTS:**
The DBT parameters for all subjects were within the normal range for the age of the subjects. None had any abnormal values. The DBT parameters for all the subjects as measured by the I-EHR and E/I ratio when correlated with time domain indices - SDNN (ms), RMSSD (ms), pNN50 and frequency domain indices- HF power (ms²) and Total power (ms²), did not show any correlation (Table 1).

**DISCUSSION:**
Our study explored the relationship between a commonly performed bedside test of Cardiac Autonomic function, the Deep Breathing Test and short term HRV indices that reflect activity of purely the parasympathetic arm of the cardiac autonomic supply as well as the indices which reflect the combined modulation of both arms of the cardiac autonomic supply. The findings of our study did not show any correlation between the absolute values of HR response to DBT and the short term HRV indices.
considered. Even though all the normal subjects had I-EHR 15bpm and E/I ratio 1.21, there was variation in the absolute values for each subject. But, this inter individual variation did not show any significant correlation with their resting spontaneous short term HRV indices. The implication of our study is that there is no relationship between the inherent spontaneous cardiac autonomic activity and the Deep Breathing Test values in our subjects. This is true of our study while considering the parasympathetic activity alone as well as the combined activity of both parasympathetic and sympathetic arms. From this we can infer that the DBT value of a person does not predict the HRV indices. However, the results of the present study is contrary to the established line of thinking that Sinus Arrhythmia by itself is a measure of HRV. There may be several reasons contributing to this contradiction. DBT has to be done properly with the subjects inspiring and expiring to the full extent of 5 second duration. Subjects in the current study may not have performed it to the full extent. Moreover, if the subjects breathe too deeply over the one minute, carbon dioxide wash out can occur producing hypocarbia and alkalosis which inturn can affect the heart rate and the extent of sinus arrhythmia and thus be a confounder(11). Another reason could be the high degree of variations in the HRV indices.There is a wide range for the normal value of the various HRV indices (6). Further, even though we attempt to measure the resting spontaneous HRV of a subject, often the subject, though physically rested might be mentally active which would affect the resting heart rate and hence the spontaneous HRV. The finding of our study nevertheless, is in line with the findings of a previously published study where the cardiac parasympathetic function test results were correlated with the power spectral indices (6). In this study, the data was collected from a heterogenous group of male subjects ranging in age from 18 years to 80 years and a statistically significant correlation was observed between the DBT values and the absolute value of HF power when no adjustment was made for age. On adjusting for age, no correlation was seen between the DBT values and the HF power. This is expected as it is known that as age advances, both HRV and extent of Sinus arrhythmia reduces (1,12). In our study, the subjects were all males with a narrow age range, extending from 25 to 35 years; hence even without adjusting for age we found no correlation between DBT values and HF absolute power. Neither was there

<table>
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<tr>
<th>HRV Parameter</th>
<th>I-EHR (n=22)</th>
<th>E/I ratio (n =22)</th>
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<tbody>
<tr>
<td></td>
<td>r value</td>
<td>p value</td>
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<tr>
<td>SDNN (ms)</td>
<td>0.23</td>
<td>0.09</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>0.31</td>
<td>0.21</td>
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<tr>
<td>pNN50</td>
<td>0.35</td>
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<tr>
<td>HF (ms²)</td>
<td>0.42</td>
<td>0.29</td>
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<tr>
<td>Total power (ms²)</td>
<td>0.32</td>
<td>0.16</td>
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our study did not find any correlation between the DBT results (I-EHR and the E/I ratio) and the short-term HRV indices reflecting either parasympathetic activity alone or combined.

REFERENCES:


