Interactive Effects of Simultaneously Varying Respiratory Frequency and Tidal Volume on Respiratory Sinus Arrhythmia

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Abstract

The effects of respiratory frequency (RF) and tidal volume (TV) on respiratory sinus arrhythmia (RSA) have been established separately. We assessed the interactive effects of simultaneously varying RF and TV on high-frequency power of RR intervals (HF RR). 25 subjects performed three 30-s breathing protocols: linearly increasing RF (RF LI) at fixed TV; linearly increasing TV (TV LI) and decreasing TV (TV LD) at fixed RF, and RF LI with TV LI-TV LD. From time-frequency spectra, HF RR and instantaneous RF were computed. RF LI-HF RR correlations were strong in separated and combined conditions, with greater regression slope in combined (p<0.001). Three types of TV LI-HF RR relations were found: negative linear, no change and positive linear. Combined protocol transformed this inconsistent response into a systematic negative linear relation with greater slope (p<0.001). TV LD-HF RR correlations were strong in separated and combined conditions, with steeper slope in combined (p<0.001). Our fast, non-fatiguing and linearly varying protocols document that: 1) RF LI consistently attenuates RSA, 2) the separate effects of TV LI-TV LD, especially TV LI, on RSA, are ambiguous and present hysteresis, and 3) RF LI combined with TV LI-TV LD induce greater attenuating effects on RSA. The nonlinear effect of TV on RSA questions the usual practice of normalizing RSA for TV.

1. Introduction

Voluntary control of respiratory movements is a powerful procedure that has permitted to explore the independent effects of respiratory frequency (RF) and tidal volume (TV) on respiratory sinus arrhythmia (RSA) magnitude, knowledge required for a comprehensive understanding of its underlying mechanisms [1,2].

Hirsch & Bishop [2] published one of the most influential studies that documented the effects of RF and TV on RSA magnitude, in which two different controlled-breathing protocols were employed: one to examine the effect of about 16 different RF at fixed TV, and the other to assess the effect of six levels of TV, at constant RF. Their results demonstrated that RSA amplitude presents an inverse relation with RF and a positive linear relation with TV, the latter being a necessary condition for normalizing RSA by TV. The findings of that study on the separated effects of each respiratory parameter on RSA have been confirmed repeatedly [3], more often for RF than for TV. However, there are no reports available documenting the effects of the simultaneous variation of the two respiratory variables on RSA amplitude. Therefore, our aim was to assess the interactive effects of the joint variation of RF and TV on the high-frequency power of RR intervals (HF RR).

2. Methods

2.1. Subjects

Twenty five healthy and sedentary subjects, 13 men and 12 women, participated. Mean age, height and weight were 23.5±1.5 years, 168±7 cm and 65.4±8.0 kg respectively. Their written informed consent was requested to participate.

2.2. Protocol

In a first visit to the laboratory health status of the subjects was assessed and they were trained to execute breathing maneuvers correctly. In a second visit, subjects performed three 30-s breathing maneuvers in random order, with 5-min resting periods in between. They were: linearly increasing RF (RF LI) from 0.15 to 0.5 Hz at a constant TV of 1L; linearly increasing TV (TV LI) from 1 to 2.5L followed by linearly decreasing TV (TV LD) from 2.5 to 1L at a fixed RF of 0.2Hz, and the simultaneous performance of RF LI and TV LI-TV LD. Maneuver execution was visually guided by displaying on a screen the target respiratory pattern and the TV of the subject.

2.3. Recorded variables and signal acquisition

ECG was detected at the thoracic bipolar derivation CM5 with a bioelectric amplifier (Biopac Systems). TV
was computed by a set of pneumotachometer (Hans Rudolph), pressure transducer (Validyne), carrier demodulator (Validyne) and integrator (Validyne). CO₂ concentration was measured with an infrared analyzer (Biopac Systems). Signals were digitized at 500 Hz via an acquisition and display system (Biopac Systems).

2.4. Data processing

R-wave peaks were detected to form RR interval series (RRi), which, together with the TV series, were cubic-spline interpolated, resampled at 8 Hz and detrended. RRi and TV time-frequency spectra were estimated via the smoothed pseudo-Wigner-Ville distribution to compute HFRR power and instantaneous RF in the 0.15-0.5 Hz frequency band. From maximum values of CO₂ recordings end-tidal CO₂ levels were computed. For visualization purposes the individual continuous dynamics and relationships were ensemble-averaged.

2.5. Statistical analysis

For classification and comparison purposes, the relations of HFRR with TV were divided into the increasing and decreasing parts. After natural logarithmic transformation, linear regressions and correlation coefficients were computed for the individual RF⁻¹-lnHFRR, TVLI-lnHFRR and TVLD-lnHFRR relationships, in both separated and combined conditions. Student’s paired t-test was employed to compare the slopes and intercepts. Statistical significance was accepted at p < 0.05.

3. Results

![Figure 1](image1.png)

Figure 1. Time course of the ensemble averages of the TV (thin line) during the three breathing protocols in relation to their respective target respiratory patterns (thick line): (A) RFli at fixed TV, (B) TVLI-TVLD at fixed RF and (C) RFli and TVLI-TVLD combined.

![Figure 2](image2.png)

Figure 2. Representative time-frequency distributions of RRi series during the three protocols: (A) RFli at fixed TV, (B) TVLI-TVLD at fixed RF and (C) RFli and TVLI-TVLD combined.

RF⁻¹-lnHFRR, TVLI-lnHFRR and TVLD-lnHFRR relations showed strong correlations in both the independent and combined protocols (Table 1), which were greater for the latter (p<0.001). The effect of RFli on lnHFRR was a systematic linear decrease in both the independent and combined protocols, with greater slope (p<0.001) in the latter (Table 1, Fig. 3 A).

The effect of TVLI-TVLD on lnHFRR was complex, especially during the TVLI part of the independent protocol, which produced three types of responses: in 34% of the recordings lnHFRR presented a progressive increase (Fig. 3B), in 24% lnHFRR power did not change (Fig. 3C) and in 42% a linear decrease was observed (Fig.
These diverse effects contrast with the systematic linear decrease of lnHF<sub>RR</sub> during the TV<sub>LD</sub> part.

Table 1. Mean ± SD of correlations, slopes and intercepts of the HF<sub>RR</sub> - respiratory variables relations during the independent (I) and combined (C) protocols. N=25.

<table>
<thead>
<tr>
<th>Relation</th>
<th>Protocol</th>
<th>Correlation</th>
<th>Slope</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF&lt;sub&gt;LI&lt;/sub&gt;</td>
<td>I</td>
<td>-0.8±0.2</td>
<td>-6.0±3.2</td>
<td>9.1±0.9</td>
</tr>
<tr>
<td>lnHF&lt;sub&gt;RR&lt;/sub&gt;</td>
<td>C</td>
<td>-0.9±0.1*</td>
<td>-12.5±4.5*</td>
<td>10.7±1.4</td>
</tr>
<tr>
<td>TV&lt;sub&gt;LI&lt;/sub&gt;</td>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>-0.8±0.2</td>
<td>-0.9±0.7</td>
<td>9.0±1.6</td>
</tr>
<tr>
<td>lnHF&lt;sub&gt;RR&lt;/sub&gt;</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>-0.0±0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>0.7±0.2</td>
<td>0.6±0.4</td>
<td>7.4±1.0</td>
</tr>
<tr>
<td>TV&lt;sub&gt;LD&lt;/sub&gt;</td>
<td>I</td>
<td>0.7±0.2</td>
<td>0.9±0.5</td>
<td>6.3±1.4</td>
</tr>
<tr>
<td>lnHF&lt;sub&gt;RR&lt;/sub&gt;</td>
<td>C</td>
<td>0.8±0.1*</td>
<td>1.8±1.0*</td>
<td>3.0±2.3*</td>
</tr>
</tbody>
</table>

*<em>p</em>&lt;0.001 between I and C protocols

The simultaneous variation of RF and TV provoked a complex response on lnHF<sub>RR</sub> power, particularly because of the much greater hysteresis it produced, reflected by the intercept differences (Table 1, Fig. 3).

The linear regression of lnHF<sub>RR</sub> in the TV<sub>LI</sub> part of the combined protocol presented a negative slope, while the slope of the regression during the TV<sub>LD</sub> section was positive (Table 1, Fig. 3B,C,D). The combined protocol induced a steeper slope (<em>p</em>&lt;0.001) on the RF<sub>LI</sub>-lnHF<sub>RR</sub> regression than the independent ones (Table 1, Fig. 3A). The combined maneuver produced a systematically negative slope on the TV<sub>LI</sub>-lnHF<sub>RR</sub> regression, steeper (<em>p</em>&lt;0.001) than any of the slopes corresponding to the diverse cases of the independent protocol (Table 1). The TV<sub>LD</sub>-lnHF<sub>RR</sub> slope of the combined protocol was also greater (<em>p</em>&lt;0.001) than the independent one (Table 1).

The independent effects of RF on RSA have been studied with protocols that change RF within a range in two modalities: pseudo-random fluctuations [4] and stepwise increments [5]. In the first type of protocol, which is difficult to perform, TV is not controlled. The second protocol is very fatiguing, since up to 13
discontinuous RF are maintained for several minutes [6].
In contrast, the RF LI protocol used in the present study is
easy to perform and includes a wide range of continuous-
and linearly varying RF in a short time, thus minimizing
the hypertentional and fatigue.

The studies aimed at establishing the effect of TV on
RSA have used similar protocols, which consist in at least
six maneuvers with increasing TVs at fixed RF, each
maintained for several minutes [1,7]. In contrast, in our
fixed RF protocol, TV is linearly increased until a
maximum, and then linearly decreased, in a breath-by-

breath manner. Given its short duration it is non-fatiguing
and relatively easy to perform. Even more, by increasing
then decreasing TV, this maneuver is capable to establish
the hysteresis of the response of the system.

All the breathing protocols we used are associated to
slight but significant hypocapnia, greatest for the
combined protocol. Although it is unlikely that such
levels of CO2 could have affected the autonomic function
[8], we cannot discard its effect.

The inversely proportional relationship between HF RR
and RF, referred to as the low-pass filter effect of the
autonomic-sinus node system, is well documented [3,4].
The continuous relationship found with our RF LI protocol
is similar to the reported ones. Therefore, the attenuation
of RSA amplitude caused by increasing RF is a markedly
consistent effect.

It is commonly accepted that RSA increases in
proportion to TV increment. The linearity of this
relationship is the supporting premise of the
normalization of RSA amplitude with TV, which is
performed using various techniques [3,7]. With our TV LI-
TV LD protocol we did not find a systematic
behavior for the TV LI-lnHF RR relation. The participants
of this study responded to the independent TV LI either with
the hyperventilation and fatigue.

The continuous relationship found with our RF LI protocol
is similar to the reported ones. Therefore, the attenuation
of RSA amplitude with TV LI-lnHF RR into a response pattern: a linear attenuation
of RSA with TV LI (negative slope) and a linear decrease
with TV LD (positive slope), which presents much greater
hysteresis. These may reflect that the inhibitory effect of
RF LI on lnHF RR first predominates over the effects of
TV LI and after is added to the inhibitory effect of TV LD.

In conclusion our fast, non-fatiguing and linearly
varying controlled breathing protocols allowed us to
document that: 1) RF LI consistently attenuates RSA,
whether applied alone or in simultaneous variation with
TV; 2) the independent effects of TV LI-TV LD on RSA are
ambiguous, especially for TV LI, and present hysteresis,
and 3) RF LI and TV LI-TV LD combined induce greater
attenuating effects on RSA than separately. The non
linear effect of TV on RSA upon we found questions the
usual practice of normalizing RSA amplitude with TV.

Acknowledgements

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