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RELATIVE TIMING OF INSPIRATION AND EXPIRATION AFFECTS RESPIRATORY SINUS ARRHYTHMIA

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SUMMARY

1. The effect of a variation in inspiration and expiration times on heart rate variability was studied in 12 healthy subjects (mean age 30±6 years; five females).

2. Two 2 min trials of controlled breathing, with either short inspiration followed by long expiration or long inspiration followed by short expiration, were compared. Average expiration/inspiration time ratios were 1.0 and 3.4, respectively. The respiration rate in both trials was approximately 10 cycles/min.

3. In trials with short inspiration followed by long expiration, respiratory sinus arrhythmia (RSA; as measured by mean absolute differences and by the high frequency band) was significantly larger than in trials with long inspiration followed by short expiration. This effect could not be accounted for by differences in respiration rate or respiratory amplitude. The higher RSA during fast/slow respiration is primarily due to a more pronounced phasic heart rate increase during inspiration, indicating that inspiratory vagal blockade is sensitive to the steepness of inspiration.

4. Respiration rate and tidal volume are respiratory variables known to modulate RSA. The results of the present study indicate that RSA can also be modulated by a third respiratory variable, the expiratory/inspiratory time ratio.

Key words: expiration time to inspiration time, heart rate variability, respiration, respiratory sinus arrhythmia, respiratory time ratio.

INTRODUCTION

Two major respiratory variables are known to influence the amplitude of respiratory sinus arrhythmia (RSA): respiration rate and tidal volume. Whereas an increase in respiration rate is associated with a decrease in RSA, an increase in tidal volume is paralleled by an increase in RSA.[1–3]

However, previous research has also hinted that within-cycle respiratory time variables may have an impact on heart rate variability (HRV). In a study investigating the effect of deep inspiration on different autonomic variables, it was found that a deep and fast inspiration has a different effect on heart rate than a deep and slow inspiration.[4]

Studies have also shown that holding one's breath between inspiration and expiration produces bradycardia,[5,6] although the breath-holding pauses in these studies markedly exceeded possible postinspiratory pauses in normal breathing. Nevertheless, Grossman[7] commented that, in addition to a slow and deep breathing pattern, a brief pause between inspiration and expiration could augment RSA.

Respiration time variables also interact with autonomic activity, subjective arousal ratings and emotions.[8] Cappo and Holmes[9] found that a voluntary prolongation of the expiratory phase of the respiratory cycle causes a reduction in psychological (determined by Likert scales) and some aspects of physiological arousal induced by the threat of electric shock. The physiological variable found to respond to the respiratory manipulation was skin resistance; heart rate and blood pressure showed no response. In a different study, an effect of passive stress on respiratory times was observed.[10] It was found that during presentation of a stress movie, expiration times were longer and postexpiration pauses were shorter than during presentation of a neutral movie. In a review of the literature, Boiten *et al.*[11] observe that mild stress, produced by mental arithmetic or negative film clips, was associated with a reduction of the post-expiratory pause.

The present study investigated the effect of the ratio of expiration time to inspiration time (E/I-ratio) on respiratory sinus arrhythmia, keeping respiration rate constant. On the basis of the results of a pilot study, it was assumed that a voluntary manipulation of this ratio (long inspiration followed by short expiration compared with short inspiration followed by long expiration) would have an impact on RSA. This would have serious implications for the measurement of vagal tone from RSA.

METHODS

Subjects

Twelve non-smoking volunteer subjects (five females) participated in the study. Their mean age was 30±6 years, the youngest being 23 and the oldest 42 years. The subjects were healthy and non-obese and were not taking any medication at the time of the study. Subjects did not consume caffeinated beverages in the 3 h before the experiment and were in sinus rhythm. All experiments were performed between 11.00 and 19.00 h and 2–5 h after the last meal.

Procedure

Subjects were informed about the aims of the study and were seated in a recliner in a quiet room. After placement of the necessary sensors, subjects were trained in controlling their E/I-ratio with the help of a biofeedback

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system (Insight Instruments, Vienna, Austria) that monitored their respiration. They were taught either to inspire slowly and then expire rapidly or to inspire rapidly and then expire slowly. The training phase lasted a maximum of 30 min. Thereafter, a 30 min experimental session began. After 8 min baseline, half the subjects were asked to inspire slowly and expire rapidly for 2 min and the other half were given the opposite instruction. Subjects received visual feedback of their abdominal excursions as a measure of their respiratory pattern. After a 3 min rest, the instructions were reversed. This procedure was repeated after a 5 min rest. The instruction to alter the respiratory pattern was always given approximately 15 s before the trial, so as to give subjects enough time to adapt their breathing pattern.

Measures

Inter-beat intervals (IBI) were measured with an electrocardiogram (ECG) instrument (Physio-Logger; Natic Co., Munich, Germany). Heart rate and a measure of respiratory sinus arrhythmia (log RSA) were calculated, the latter using the method of Moser *et al*.[12,13] The calculation was conducted as follows: the IBI were converted to heart rate and the absolute heart rate differences (in b.p.m.) from one heart beat to the next were calculated for 1 min periods. This procedure acts as a high-pass filter that passes the high-frequency variations attributed to RSA but not the slow variations originating from combined sympathetic and parasympathetic activity. The median of the absolute beat-to-beat differences was next transformed by taking its logarithm. This method was originally described by Eckoldt[14] and modified by Moser *et al*.[13] The logarithm was chosen because the individual median values are not distributed normally, but as a log-normal distribution. The logarithmic transformation of the medians produces a normal distribution. LogRSA was chosen as an indicator of vagal tone because it is easy to calculate and is highly correlated with the spectral estimation of cardiac vagal tone during spontaneous respiration ($r = 0.88$; $n = 220$; M Moser *et al*., unpubl. obs., 1998). A similar method is described by McCarty and Watkins[15] for the IBI.

Additionally, the spectral density of HRV in the high-frequency band (0.38–0.14 Hz, corresponding to 8.4–22.8 respiratory cycles per minute), middle-frequency band (0.14–0.07 Hz) and low-frequency band (0.07–0.025 Hz) was calculated using the method of Berger *et al*.[16] The high-frequency band was chosen to monitor vagal activity in correspondence with the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.[17]

As a measure of the steepness of heart rate change, the average increase of IBI, as well as the average decrease of IBI, were calculated for the three conditions. This was done by subtracting consecutive IBI and grouping them according to the resulting sign (increase or decrease). The absolute value was taken for negative differences. Greater values of the two resulting measures stand for steeper increases or decreases of IBI, respectively.

Respiration was measured by using strain gauges around the thorax (placement in the middle of the sternum) and the abdomen (placement 2 cm above the navel). Inspiratory and expiratory durations, their ratio and respiration rate were derived from thoracic movements. The inspiratory duration was defined as the time between the beginning of the onset of inspiration and the end of inspiration. Expiratory duration was defined as the time between the end of inspiration and the beginning of the next inspiration. Using this definition, the expiratory phase encompasses not only the expiration time but also the inspiratory and expiratory pause. This procedure was chosen because of the greater stability of the inspiratory phase in the respiratory cycle compared with the expiratory phase. Respiratory amplitudes were determined for both thoracic and abdominal movements. All respiratory variables were computed on-line. Pulse volume amplitude (PVA) was measured using infrared plethysmography on the fourth finger of the non-dominant hand.

Statistics

The log RSA, heart rate, the upper and lower octile of heart rate and the average IBI increase and decrease were calculated for consecutive minutes from the sequence of IBI. Respiratory measures and PVA were automatically determined by the hardware and 1 min medians of 5 s averages were calculated. From these data, the E/I-ratio, respiration rate, respiration amplitude and PVA were calculated. As the baseline value, the average of the baseline minutes 5–7 was taken. The averages of the four minutes of the short inspiration and long expiration (SILE) phase and the long inspiration and short expiration (LISE) phase were taken as values of the appropriate trials. Data were analysed by the use of paired *t*-tests and Pearson's correlations.

RESULTS

Figure 1 provides three representative samples of heart rate variations during baseline, LISE and SILE. It can be seen that during the SILE breathing pattern, RSA amplitudes are increased relative to baseline, whereas during the LISE breathing pattern amplitudes are not different from or even decreased in comparison with baseline. During SILE breathing, the heart rate increase occurs rapidly, whereas during LISE breathing the heart rate increase is less pronounced.

In Table 1, the mean values of baseline, LISE and SILE are listed. As expected, the two trials differ significantly in the E/I-ratio

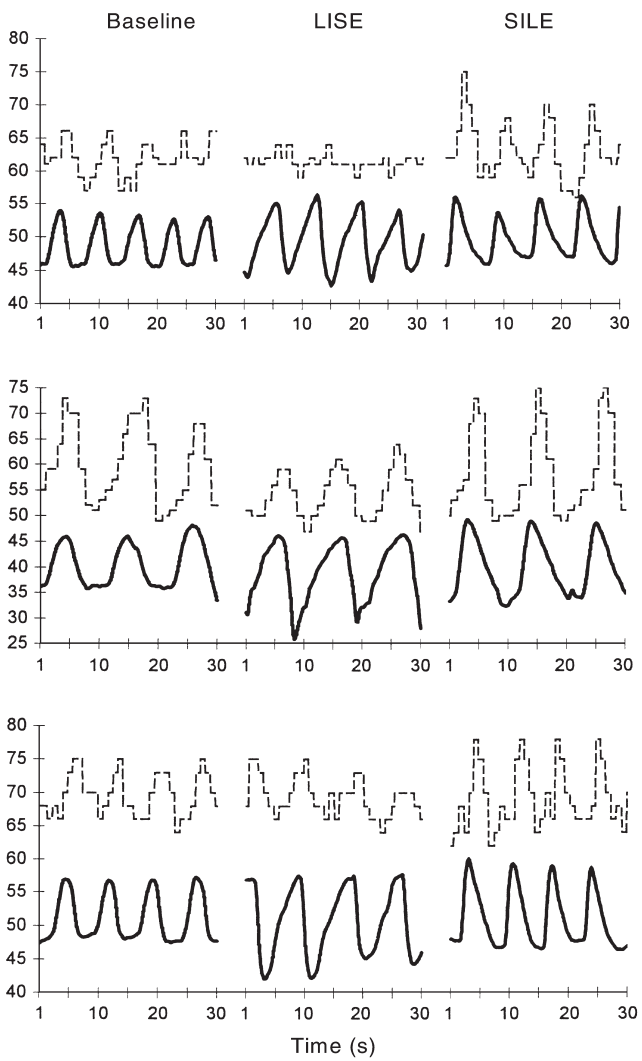

Fig. 1 Representative samples of heart rate (-----; b.p.m.) and respiration (——; arbitrary units) during baseline, long inspiration followed by short expiration (LISE) and short inspiration followed by long expiration (SILE) in three different subjects (subject a, top traces; subject b, middle traces; subject c, bottom traces).

Table 1 Mean values and statistics of measured variables

	Baseline	LISE	SILE	*P* base–LISE	*P* base–SILE	*P* SILE–LISE
Respiration rate (counts/min)	12.8±2.8	9.6±3.1	10.0±3.1	**	**	
Respiration amplitude						
Thorax	9.1±3.6	14.7±4.8	15.4±7.5	**	**	
Abdomen	33.1±18.5	62.6±33.8	43.0±18.6	**	*	*
E/I-ratio	1.8±0.3	1.0±0.3	3.4±0.8	***	***	***
Mean IBI increase (msec)	26.5±8.6	33.4±20.4	37.5±18.0		*	
Mean IBI decrease (msec)	28.2±10.9	27.3±15.1	40.7±16.4		**	***
Heart rate (b.p.m.)	70.6±12.3	68.9±9.3	70.4±10.9			*
Heart rate upper octil	75.3±12.4	74.7±10.3	77.6±12.1		*	***
Heart rate lower octil	66.4±11.5	63.8±9.3	64.3±10.1	*		
log RSA (log(b.p.m.))	0.22±0.15	0.22±0.22	0.39±0.22		**	***
HF (0.14–0.38 Hz)	6.70±5.40	10.2±15.6	17.1±20.8		**	**
MF (0.07–0.14 Hz)	8.2±9.3	18.9±21.8	25.2±24.6		*	
LF (0.025–0.07 Hz)	8.1±9.3	6.3±4.5	7.7±8.3			
PVA	71.9±40.2	61.4±36.6	55.9±33.2		**	*

Data are the mean±SD. The significance levels pertain to *t*-tests for the differences between conditions. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

E/I-ratio, ratio of expiration time to inspiration time; IBI, inter-beat intervals; RSA, respiratory sinus arrhythmia; HF, high frequency; MF, middle frequency; LF, low frequency; PVA, pulse volume amplitude; LISE, long inspiration followed by short expiration; SILE, short inspiration followed by long expiration.

($P < 0.01$), illustrating that the experimental manipulation of the respiratory pattern was successful. In the LISE trial, the ratio was 1.0, whereas in the SILE trial the ratio was 3.4. The expiratory to inspiratory time ratio during baseline was 1.8, indicating that, at rest, expiration is longer than inspiration. Due to the determination of the respiratory durations, the inspiration time is probably slightly underestimated and the expiration time slightly overestimated (see Methods).

The E/I-ratio was approximately 3.4-fold larger in the SILE than the LISE condition. For the average respiratory cycle, this means that inspiratory times were either 1.4 s (SILE) or 3.1 s (LISE) and expiratory times were 4.6 s (SILE) or 3.2 s (LISE), respectively. Therefore, the variations of the E/I-ratio were accounted slightly more by variations of the inspiration time (1.7 s difference between SILE and LISE) than by variations of the expiration time (1.4 s difference). In the SILE trial, the E/I-ratio was significantly lower than during baseline, whereas in the LISE trial, the ratio is significantly higher than during baseline. This implies that the respiratory pattern was altered successfully in both trials compared with the baseline level. The two trials did not differ with respect to respiration rate or thoracic respiratory amplitude, but abdominal respiratory amplitude was significantly larger during the LISE trial than during the SILE trial.

As can be seen in Fig. 2, log RSA was significantly higher during trials of short inspiration followed by long expiration (SILE) than during trials of long inspiration followed by short expiration (LISE; $P < 0.001$). This difference is caused by an increase in log RSA from baseline to SILE, whereas log RSA did not decrease in LISE compared with baseline. The spectral analysis data of the heart rate time series reveal a similar finding. The power of the high-frequency band, which corresponds to respiratory modulation of heart rate, was significantly higher in the SILE than LISE condition. The correlation between the power of the high-frequency band and the log RSA measure used is $r = 0.64$ ($P < 0.05$). In contrast, there is no difference between the trials with respect to the power of the middle-frequency and low-frequency bands, although the middle-frequency band does increase in power significantly from baseline to the SILE condition.

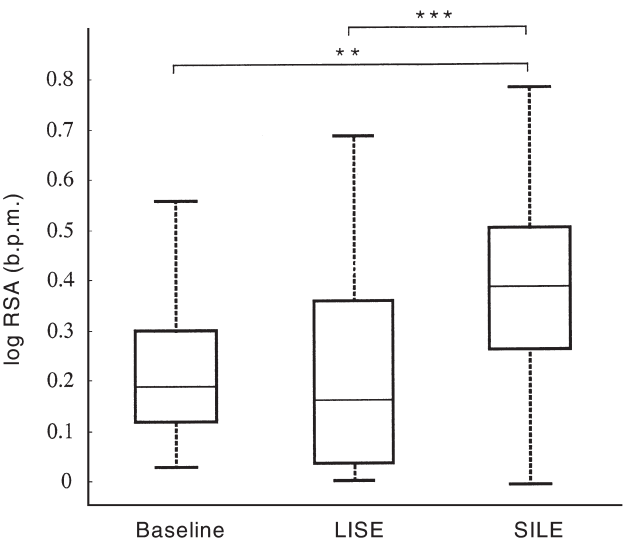

Fig. 2 Box-plots of log respiratory sinus arrhythmia (RSA) during baseline, long inspiration followed by short expiration (LISE) and short inspiration followed by long expiration (SILE). **$P < 0.01$, ***$P < 0.001$.

Changes in consecutive IBI were affected differently by the two conditions (Table 1). In the SILE condition, the average IBI decrease was significantly greater than in the LISE condition ($P = 0.001$). This indicates that greater phasic heart rate increases occurred in the SILE condition compared with the LISE condition. No differences were found between the SILE versus LISE conditions with regard to the average IBI increase, indicating that phasic heart rate decreases were similar in both conditions. Both average IBI increases and decreases were greater in the SILE condition than during baseline.

Average heart rate was lower in the LISE condition than in the SILE condition ($P < 0.05$, *t*-test, 11 d.f.). This difference was due

Table 2 Correlation between heart rate variability and respiration across subjects

	log RSA	LF	MF	HF
Respiration rate	–0.0346	0.4329	–0.2204	–0.2462
Expiration time/ inspiration time	0.3876	0.0755	–0.4629	0.2017
log RSA	–	–0.1789	0.0814	0.6440*

The correlations were calculated with baseline values. *$P < 0.05$.

RSA, respiratory sinus arrhythmia; LF, low frequency; MF, middle frequency; HF, high frequency.

Table 3 Correlations between changes in log respiratory sinus arrhythmia with changes in respiration

Δ Variable from baseline to trial	SILE Δ log RSA	SILE *P*	LISE Δ log RSA	LISE *P*
Δ Respiration rate	–0.59	0.04	–0.68	0.02
Δ Respiration amplitude				
Thorax	0.56	0.06	0.41	NS
Abdomen	0.02	NS	0.05	NS

Changes from baseline to trials were both calculated for short inspiration followed by long expiration (SILE) and long inspirations followed by short expiration (LISE) trials.

RSA, respiratory sinus arrhythmia.

primarily to differences in maximum heart rate and not in minimum heart rate values, because the upper octile of heart rate in the SILE condition was higher than that in the LISE condition, but for the lower octile, heart rate did not differ significantly between the two conditions. Similarly, although there were no differences in mean heart rate between trials and baseline, the upper octile of heart rate was higher ($P < 0.05$, *t*-test, 11 d.f.) in the SILE condition than during baseline, which is consistent with the previously mentioned observation that short inspiration increases heart rate phasically. In both trials, lower octile heart rate was lower than that of baseline, although this difference was statistically significant only for the LISE trial.

Pulse volume amplitude, measured from the finger pulse, was lower in the SILE than the LISE condition. In addition, PVA was significantly lower in the SILE condition and numerically lower in the LISE condition than during baseline.

To test for possible covariations between the respiratory pattern and HRV at rest, a correlation analysis was calculated between respiration rate and the E/I-ratio on the one hand and log RSA and the power of low-, medium- and high-frequency spectra on the other (Table 2). The correlations were calculated with the baseline values across subjects ($n = 12$). Neither respiration rate nor the E/I-ratio correlated significantly with any of the HRV variables. There was a significant positive correlation between log RSA and the power of the high-frequency band, but not with the other two frequency bands.

To analyse the effects of the experimental variations of respiration on RSA apart from the E/I-ratio, correlations between changes in respiration rate and the amplitudes of thoracic and abdominal excursions from baseline to trials with changes in log RSA in the appropriate trials were calculated. As can be seen from Table 3, a decrease in respiration rate was significantly associated with an increase in log RSA. Also, an increase from baseline to trial in thoracic, but not abdominal, respiratory amplitude was associated weakly ($P < 0.06$) with an increase in log RSA, but only in the SILE condition.

DISCUSSION

The present study investigated the effect of the respiratory time ratio (E/I-ratio) on HRV. No previous studies known to the authors have addressed possible effects of breathing patterns on the amount of HRV. In contrast, the effect of respiration rate and tidal volume on RSA have been well documented[3] and are known to be confounding variables in research using RSA as a measure of cardiac vagal tone.[18]

Subjects in the present study altered their inspiration and expiration times systematically with the help of respiratory biofeedback. During trials with short inspiration followed by long expiration, RSA was higher than in trials with long inspiration followed by short expiration. This is due, at least in part, to the more pronounced phasic increase in heart rate accompanying fast inspiration than slow inspiration, as measured using the upper octiles of heart rate and the average decrease of IBI.

Because these respiratory manipulations also had a marked impact on respiration rate (which was generally lower during the trials than during baseline) and amplitude (which was generally higher during the trials than during baseline), the effect on RSA could, theoretically, result from between-trial differences in these respiratory variables. However, there is evidence that this is not the case for respiration rate: there were no differences in respiration rate between trials in spite of the observed change in RSA. Respiration rate was even numerically slightly higher in trials with higher RSA, ruling out respiration rate as a factor contributing to the observed difference in RSA between trials. The second factor that possibly could explain the observed differences in RSA is respiratory amplitude. Thoracic respiratory amplitude did not differ between the two trials. In contrast, abdominal respiratory amplitude was smaller in the trial with larger RSA. This rules out respiratory amplitude as a possible factor contributing to the observed differences, because an increase in respiratory amplitude has been shown to be associated with an increase in RSA. Therefore, we conclude that the differences in RSA are primarily due to differences in the E/I-ratio.

The manipulation of the E/I-ratio also had an effect on heart rate. Heart rate was slightly but significantly higher in the SILE trials compared with LISE trials. This is primarily due to the pronounced phasic increase in heart rate accompanying fast inspiration, which is not seen during slow inspiration. In contrast, phasic heart rate deceleration during expiration is independent of the rate of expiration. The finding of higher heart rates during trials with long expiration is in contrast with the results of a study by Cappo and Holmes,[9] who did not observe any differences in heart rate between the two respiratory manoeuvres of fast inspiration/slow expiration versus slow inspiration/fast expiration during a non-threat condition. The tonic heart rate effects found in the present study may have resulted from the large differences between the E/I time ratio in both trials. These measures where not reported in the study by Cappo and Holmes.[9]

If RSA is an index of cardiac vagal tone, as the majority of recent research shows,[19–22] then the above finding seems to be contradictory. One would expect an increase in RSA and, therefore, in cardiac vagal tone, to be accompanied by a decrease in heart rate. Two explanations of this paradox seem possible: (i) a simultaneous increase in sympathetic tone, a variable that we did not measure in this study; and (ii) an overestimation of cardiac vagal tone in the SILE condition resulting from the exaggerated phasic component of RSA due to the applied breathing protocol. Without pharmacological blockade, it cannot be decided conclusively which of these explanations is

more likely, although the observed decrease of finger pulse volume amplitude in the SILE condition indicates a simultaneous increase in sympathetic tone.

It is generally assumed that inspiration blocks the generation of cardiac vagal tone in medullary centres, whereas vagal tone is uninhibited during expiration.[20,23] The results of the present study allow further insight into this interaction. They support the hypothesis that cardiac vagal tone is blocked more during fast inspiration than during slow inspiration, with a sensitivity to the steepness of inspiration. In contrast, the opening of the vagal gate during expiration does not seem to be influenced by the steepness or duration of expiration, because the lower range of heart rate and the average increase of IBI is similar for both breathing patterns.

The differential effect of the steepness of inspiration on RSA also is supported by the study of Saul *et al*.[24] on the mechanisms generating RSA. They found that changes in arterial pressure are largest during maximal inspiratory flow, due to the fast change in intrathoracic pressure. This effect could account for the observed relationship between steepness of inspiration and heart rate change in this study, in accordance with the evidence that arterial pressure changes lead to inverse heart rate changes via the baroreceptor.[24–26]

An interesting observation in the present study is the fact that an increase of the thoracic respiratory amplitude tends to contribute more to an increase in RSA than an increase of the abdominal respiratory amplitude. This may suggest a differential effect between costal and diaphragmatic respiration on RSA, but could also be due to the specific breathing pattern generated in this study.

A possible limitation of the present study is the fact that only the effect of controlled breathing on RSA was studied and not that of spontaneous breathing. Unfortunately, it is unclear whether the voluntary control of respiration affects RSA as compared with spontaneous breathing, because studies have found conflicting results.[2,27,28] Another limitation of the present study is the fact that the effects of E/I-ratios were only studied during relatively slow breathing and increased respiratory amplitudes. Furthermore, the differences between the respiratory patterns were large, inspiration times being considerably shorter and expiration times longer in the one condition compared with the other. Therefore, it is not known whether the observed effect also is present in normal resting respiration with higher respiration rates and lower amplitudes. Also, it remains to be determined whether smaller differences in E/I-ratio alter RSA in a way similar to the presented results.

In summary, the results indicate that the ratio of expiration time to inspiration time may have an impact on RSA. This effect seems to be primarily due to a more pronounced phasic increase of heart rate during fast inspiration than during slow inspiration. Regarding the outcome of the study, the authors believe that it could be helpful to consider the effects of breathing patterns (i.e. E/I-ratio) in studies dealing with HRV.

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REFERENCES

1. Angelone A, Coulter N. Respiratory sinus arrhythmia: A frequency dependent phenomenon. *J. Appl. Physiol.* 1994; **3**: 479–82.
2. Hayano J, Mukai S, Sakakibara M, Okada A, Takata K, Fujinami T. Effects of respiratory interval on vagal modulation of heart rate. *Am. J. Physiol.* 1994; **267**: H33–40.
3. Hirsch JA, Bishop B. Respiratory sinus arrhythmia in humans: How breathing pattern modulates heart rate. *Am. J. Physiol.* 1981; **241**: H620–9.
4. Stern RM, Anschel C. Deep inspirations as stimuli for responses of the autonomic nervous system. *Psychophysiology* 1968; **5**: 132–41.
5. Ross A, Steptoe A. Attenuation of the diving reflex in man by mental stimulation. *J. Physiol.* 1980; **302**: 387–93.
6. Folinsbee L. Cardiovascular response to apneic immersion in cool and warm water. *J. Appl. Physiol.* 1974; **36**: 226–32.
7. Grossman P. Respiration, stress and cardiovascular function. *Psychophysiology* 1983; **20**: 284–300.
8. Lorig TS, Schwartz GE. The pulmonary system. In: Cacioppo JT, Tassinary LG (eds). *Principles of Psychophysiology*. Cambridge University Press, Cambridge. 1990; 580–98.
9. Cappo BM, Holmes DS. The utility of prolonged respiratory expiration for reducing physiological and psychological arousal in non-threatening and threatening situations. *J. Psychosom. Res.* 1984; **28**: 265–73.
10. Cohen HD, Goodenough DR, Witkin HA, Oltman PH, Gould H, Shulman E. The effects of stress on components of the respiration cycle. *Psychophysiology* 1975; **12**: 377–80.
11. Boiten FA, Frijda NH, Wientjes CJE. Emotions and respiratory patterns: Review and critical analysis. *Int. J. Psychophysiol.* 1994; **17**: 103–28.
12. Moser M, Lehofer M, Hoehn-Saric R *et al.* Increased heart rate in depressed subjects in spite of unchanged autonomic balance? *J. Affect. Dis.* 1998; **48**: 115–24.
13. Moser M, Lehofer M, Sedminek A *et al.* Heart rate variability as a prognostic tool in cardiology. *Circulation* 1994; **90**: 1078–82.
14. Eckoldt K. Probleme und Ergebnisse der Analyse des Sinusrhythmus. *Psychiatr. Neurol. Med. Psychol. Beih.* 1990; **43**: 53–63.
15. McCarty R, Watkins A. *Autonomic Assessment Report. Interpretation Guide and Instructions.* Heartmath Research Center, Boulder Creek, CA. 1996.
16. Berger RD, Akselrod S, Gordon D, Cohen RJ. An efficient algorithm for spectral analysis of heart rate variability. *IEEE Trans. Biomed. Eng.* 1986; **33**: 900–4.
17. 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. *Eur. Heart J.* 1996; **17**: 354–81.
18. Grossman P, Karemaker J, Wieling W. Prediction of tonic parasympathetic cardiac control using respiratory sinus arrhythmia: The need for respiratory control. *Psychophysiology* 1991; **28**: 201–16.
19. Billman GE, Dujardin JP. Dynamic changes in cardiac vagal tone as measured by time series analysis. *Am. J. Physiol.* 1990; **258**: H896–902.
20. Grossman P, Kollai M. Respiratory sinus arrhythmia, cardiac vagal tone, and respiration: Within- and between-individual relations. *Psychophysiology* 1993; **30**: 486–95.
21. Hayano J, Sakakibara Y, Yamada A *et al.* Accuracy of assessment of cardiac vagal tone by heart rate variability in normal subjects. *Am. J. Cardiol.* 1991; **67**: 199–204.
22. Porges SW. Respiratory sinus arrhythmia: Physiological basis, quantitative methods, and clinical implications. In: Grossman P, Janssen KHL, Vaitl D (eds). *Cardiorespiratory and Cardiosomatic Psychophysiology*. Plenum Press, London. 1986; 101–15.

23. Berntson GG, Cacioppo JT, Quigley KS. Respiratory sinus arrhythmia: Autonomic origins, physiological mechanisms, and psychophysiological implications. *Psychophysiology* 1993; **30**: 183–96.
24. Saul JP, Berger RD, Albrecht P, Stein SP, Chen MH, Cohen RJ. Transfer function analysis of the circulation: Unique insights into cardiovascular regulation. *Am. J. Physiol.* 1991; **261**: H1231–45.
25. Laude D, Goldman M, Escourrou P, Elghozi J-L. Effect of breathing pattern on blood pressure and heart rate oscillations in humans. *Clin. Exp. Pharmacol. Physiol.* 1993; **20**: 619–26.
26. Piepoli M, Sleight P, Leuzzi St Valle F *et al.* Origin of respiratory sinus arrhythmia in conscious humans. An important role for arterial carotid baroreceptors. *Circulation* 1997; **95**: 1813–21.
27. Patwardhan AR, Evans JM, Bruce EN, Eckberg DL, Knapp CF. Voluntary control of breathing does not alter vagal modulation of heart rate. *J. Appl. Physiol.* 1995; **78**: 2087–94.
28. Patwardhan AR, Vallurupalli S, Evans JM, Bruce EN, Knapp CF. Override of spontaneous respiratory pattern generator reduces cardiovascular parasympathetic influence. *J. Appl. Physiol.* 1995; **79**: 1048–54.