Psychological and physiological responses to stress

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Functional somatic symptoms suggestive of hyperventilation are not associated with impaired cardiorespiratory coupling

Jan H. Houtveen, Simon Rietveld, & Eco J. C. de Geus

Abstract

This study tested whether participants with functional somatic symptoms are characterized by impaired cardiorespiratory coupling. Out of 499 young, somatically healthy, female participants, the 18 women with most recent functional somatic symptoms and the 18 women with least recent functional somatic symptoms were submitted to conditions of mental stress, mild physical exercise, and relaxation during three different breathing conditions: normal breathing, breathing compressed normal air, and breathing compressed 5% CO$_2$-enriched air. Throughout, respiratory sinus arrhythmia (RSA) was measured as the high frequency heart period variability power, respiratory rate and depth were assessed by impedance cardiography, and central respiratory drive by end-tidal partial pressure of CO$_2$. Participants with functional somatic symptoms reported more base-rate tenseness, anxiety, and somatic symptoms, and these group differences increased in response to mental stress and during 5% CO$_2$ inhalation. However, no group differences were found in base-rate RSA, in the RSA-response to mental stress or physical exercise, and during 5% CO$_2$ inhalation. Also, no group differences were found in other respiratory-related physiological measures. It was concluded that functional somatic symptoms suggestive of hyperventilation are not associated with a disruption in the RSA regulatory system.
Introduction

Individuals with numerous functional somatic symptoms, that can not be explained by somatic disorders, have been frequently described in scientific literature (e.g., Da Costa, 1871; Costa & McCrae, 1985; Watson & Pennebaker, 1989; Wesseley, Nimnuan, & Sharpe, 1999). Although differences in ventilatory activity can not be completely ruled out as explanatory mechanisms for some functional somatic symptoms in some individuals (Sharpe & Bass, 1992; Troosters et al., 1999; Wientjes & Grossman, 1994), the concept of hyperventilation can generally be rejected as a causal mechanism of functional somatic symptoms (Hornsveld, Garssen, Fiedeldij Dop, van Spiegel, & Haes, 1996; Troosters et al., 1999; Wientjes & Grossman, 1994). Ambulatory transcutaneous monitoring of the partial pressure of CO$_2$, in individuals that were suspected to suffer from hyperventilation, demonstrated that episodes with symptoms were not preceded by hyperventilation (Hornsveld et al., 1996). Episodes with symptoms were only related to hyperventilation in a minority of these individuals. However, previous studies have mainly concentrated on respiratory behavior and the regulation of the arterial partial pressure of CO$_2$. Possible effects of low cardiac vagal tone or dysfunctional cardiorespiratory coupling on the regulation of arterial partial pressure of O$_2$ have not been considered.

In an ingenious study, Hayano, Yasuma, Okada, Mukai, and Fujinami (1996) demonstrated the physiological relevance function of the phasic linkage between the heart rate and the respiratory cycle, known as the respiratory sinus arrhythmia (RSA) phenomenon. They induced respiratory-linked heartbeat fluctuations in anaesthetized dogs after elimination of endogenous autonomic activities by atrial pacing. Their results demonstrated how artificially increased RSA increased the O$_2$ consumption and delivery, decreased the ratio of physiological dead space to tidal volume, and decreased the fraction of intrapulmonary shunt. Vice versa, artificially decreased RSA reduced O$_2$ consumption and delivery. No changes were observed in respiratory rate, tidal volume, cardiac output, minute heart rate, arterial blood pressure, O$_2$ saturation, and CO$_2$ tension. Hayano and co-workers (1996) concluded that RSA benefits pulmonary gas exchange by matching perfusion to ventilation within each respiratory cycle. Other animal studies also demonstrated that the most probable function of RSA is to improve the pulmonary O$_2$ transfer (see Taylor, Jordan, & Coote, 1999). RSA probably works as a fine-tuning system between respiration and pulmonary O$_2$ transfer. Such a fine-tuning system makes sense since the mammalian brain is extremely sensitive to O$_2$ deprivation.

Within-subject psychophysiological studies have demonstrated that psychological stress (Allen & Crowell, 1989; Kamphuis & Frowein, 1985; Langewitz & Ruddel, 1989) usually reduces RSA, whereas increased RSA is associated with conditions of psychological relaxation (Skakibara, Takeuchi, &
In fact, short-term reductions in RSA are a characteristic feature of the flight-flight stress response (Berntson et al., 1994; Berntson, Cacioppo, & Quigley, 1993a, 1993b; Cacioppo, 1994). Clinical studies have demonstrated that chronically reduced RSA and/or an excess in task-related reductions in RSA are associated with anxiety (Friedman & Thayer, 1998; Thayer, Friedman, & Borkovec, 1996; Watkins, Grossman, Krishnan, & Sherwood, 1998), and depression (Carney et al., 1995; Musselman, Evans, & Nemeroff, 1998). It has also been repeatedly demonstrated that anxiety and/or psychological distress are closely tied to somatic symptom complaints (Pennebaker, 1982; Watson & Pennebaker, 1989; Wientjes & Grossman, 1994). More specifically, it has been suggested that anxiety related to experienced physiological sensations increases the amount of reported somatic symptoms (Clark, 1988; Pennebaker, 1982). One hypothesis to connect the various findings above is to suggest that psychological stress and/or anxiety cause reduced RSA, and that reduced RSA causes or at least enhances functional somatic symptoms, possibly through its effects on $O_2$ regulation. The first purpose of the present study was to test a specific part of this hypothesis, namely whether individuals with numerous functional somatic symptoms are indeed characterized by low resting RSA and/or increased reduction of RSA during psychological stress.

Two manipulations that induce both increased somatic symptoms and anxiety in individuals with numerous functional somatic symptoms are hypocapnia (alkalosis) induced by voluntary hyperventilation (Hornsveld, Garssen, & van Speigel, 1995), and hypercapnia (acidosis) induced by inhalation of a CO$_2$-enriched air mixture (Van den Bergh, Stegen, & Van de Woestijne, 1997). This ties in nicely with the observation that under normal conditions, $O_2$ sensors account for only a small part of the chemical drive to breathe, whereas this so-called ‘central respiratory drive’ is very sensitive to small differences in the arterial partial pressure of CO$_2$ (Feldman & McEvedy, 1999). Therefore, although RSA helps to increase the efficiency of the pulmonary circulation and $O_2$ transfer, it is more likely to be under control of the arterial partial pressure of CO$_2$ than $O_2$. As a consequence, deviant RSA regulation in individuals with numerous functional somatic symptoms may become particularly evident during changes in partial pressure of CO$_2$. This could explain their enhanced vulnerability to experiencing complaints under such conditions, for which there is currently no available physiological explanation. The second purpose of the present study is to explore the effects of hypercapnia on the RSA regulation in individuals with numerous functional somatic symptoms. In healthy individuals, a hypercapnic state has been demonstrated to enhance RSA by enhancing the central respiratory drive (Al-Ani, Forkins, Townend, & Coote, 1996). We expect this normal increase in RSA as a result of CO$_2$-enriched air inhalation to be reduced or even reversed in individuals with numerous functional somatic symptoms.
Methods

Participants
Young women with numerous functional somatic symptoms ($n=18$) and young women without such symptoms ($n=18$), all without chronic disease, were recruited from a sample of 499 undergraduate students. Women were selected that scored equal or below the 20th percentile (value 9) and women were selected that scored equal or above the 80th percentile (value 26) on the hyperventilation symptom questionnaire, as used by Hornsveld and co-workers (1996), during a group test session. All participants completed this questionnaire (for a second time) during the experimental procedure, and all participants remained above (low in somatic symptoms; LSS group) versus below (high in somatic symptoms; HSS group) the normative median (value 16). The study was presented to them as an investigation of breathing patterns. The participants believed that they could win 100 Dutch guilders ($50), although all received a similar amount of 30 Dutch guilders ($15) after the experiment. All participants signed an informed consent. The study had been approved by the ethics committee of the department of Psychology, University of Amsterdam. None of the participants used medication excepting oral contraceptives in 25 women. The participants were instructed to refrain from eating, drinking (except for water), smoking, or physical exercise within one hour before the experiment. Technical problems resulted in the loss of physiological data from one participant.

Questionnaires
A Dutch version of the hyperventilation symptom questionnaire (HSQ) was used to select participants with numerous functional somatic symptoms and controls (see Hornsveld et al., 1996). This questionnaire has 31 items and assesses the frequency of symptoms during the past month. Ratings were made on a four-point scale (range 0-3), comprising the categories ‘did not occur’, ‘one or more times a month’, ‘one or more times a week’, and ‘daily’. The total score ranges from 0 to 93 points.

A Dutch translation of the Spielberger state-trait anxiety inventory (STAI; Spielberger, Gorsuch, & Lustene, 1970; van der Ploeg, 1981) was used to measure trait anxiety. This questionnaire has 20 items, and the total score ranges from 20 to 80 points.

Procedure
The experiment consisted of three conditions that were conducted in fixed order: (1) a mental stress task, (2) a ‘relaxation’ condition, and (3) mild physical exercise. Each of these conditions consisted of three parts of 4 minutes each, again
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conducted in fixed order: (a) breathing normally, (b) breathing compressed normal air through a face mask, and (c) breathing compressed 5% CO₂-enriched air through a face mask. All experimental sessions took place between 11 AM and 4 PM, and lasted approximately 2.5 hours.

After general instructions, the recording electrodes were attached and connected to the Vrije Universiteit Ambulatory Monitoring System (VU-AMS version 4.3; see below). Next, the participants went into a waiting room for 15 minutes to relax, during which they were quietly sitting, they completed the questionnaires, and they read a popular magazine. Next, they entered the experimental room that was sound shielded and dimly lit. The Ambulatory Monitoring System was connected to an MS-DOS computer, and the participants were attached to the Pet-CO₂ recording equipment (see below). Next, participants had to rate their experienced symptoms, after which the mental stress task was started on the MS-DOS computer. Intelligence test questions were presented one by one on the middle of the screen. The maximum time for each question was 60 seconds and the elapsed time was visible on screen. The participants selected one of five multiple-choice responses (1 to 5) and pressed the corresponding key on the PC-keyboard. A simultaneously presented reaction time task consisted of random timed falling red and green coins on the left and right side of the screen. The participants were instructed to press the left button (located at the left side of the keyboard) when a green coin was falling on the left side, and to press the right button (located at the right side of the keyboard) when a green coin was falling on the right side. The computer acknowledged each response (or lack of response) with a brief auditory signal: a musical tone indicating a correct response and a low frequency buzz indicating error. The combined score on intelligence and reaction time tasks was expressed in Dutch guilders on screen. The initial amount was 100 Dutch guilders ($50), which gradually diminished as a result of the errors made. Real bank notes were placed in front of the participants before the task started, and withdrawn when lost. Two research assistants observed the participants and their performance at close distance to increase the stressfulness of the task. After 4 minutes, the task stopped and participants again rated their experienced symptoms. Next, the same task continued, but participants (additionally) had to breathe compressed normal air through a face mask (4 minutes). After 4 minutes, the task stopped again and participants (again) rated their experienced symptoms. Next, the same task continued, but participants had to breathe compressed CO₂-enriched air through a face mask (4 minutes). Finally, after participants again rated their experienced symptoms, the Pet-CO₂ recording equipment was disconnected and the participants were debriefed about the stress induction and accompanied to the waiting room.

After a new 15 minute period of quiet sitting and reading, the participants re-entered the experimental room for the ‘relaxation’ condition. The VU-AMS was again connected to the MS-DOS computer and the participants were again attached to the Pet-CO₂ recording equipment. This condition was not different
from the previous relaxation (i.e., the participants quietly sat reading a popular magazine), but after 4 minutes, they (additionally) had to breathe compressed normal air through a face mask (4 minutes), and they had to breathe compressed CO₂-enriched air through a face mask (4 minutes). The participants rated their experienced symptoms at the same moments as during the stress induction (i.e., before and after each 4 minutes period).

Before the final exercise condition, participants again relaxed in the waiting room for 15 minutes. After they had returned to the experimental room, the VU-AMS was again connected to the MS-DOS computer, and the participants were again attached to the Pet-CO₂ recording equipment. Next, the participants cycled on a bicycle home-trainer, which was set at minimal resistance, while watching the computer screen. A feedback procedure was used to ensure that the same increase in heart rate was obtained (for each participant) during exercise as during mental stress. The participants were instructed to cycle faster or slower in such a way that the top of the bar on the screen was as close as possible to a set-point indicated by a line. The height of the bar represented their mean heart rate over the previous 10 seconds, and it was updated every 4 seconds. Participants were kept unaware that the height of the bar reflected their current heart rate, and that the line reflected their (previous measured and saved) mean heart rate during the corresponding part of the mental stress task. The participants' body posture during this bicycle task was fairly similar to their posture during the mental stress and relaxation tasks. After 4 minutes, they again (additionally) had to breathe compressed normal air through a face mask (4 minutes), and they had to breathe compressed CO₂-enriched air through a face mask (4 minutes). The participants rated their experienced symptoms at the same moments as during the stress induction and during relaxation (i.e., before and after each 4 minute period).

Finally, all equipment was disconnected, electrodes were removed, participants were debriefed, paid, and sent home.

*Compressed normal air and 5% CO₂-enriched air breathing*

Compressed normal air and CO₂-enriched air were stored in two cylinders, which were located in an adjacent room. One cylinder contained medical air and the other a mixture of medical air and CO₂. Each cylinder had its own flow regulation as well as a moisturizing device. The air flow from both cylinders was connected by a T-piece to a single silicon tube with an inner diameter of 7 mm, and a length of 4 meters, of which one meter came out in the experimental room. This end was fed into a silicon air reservoir, in turn connected (via a silicon tube of 32 mm inner diameter and a length of 50 cm) to a silicon half face mask (Dräger Combitox Nova RA). This non-leaking mask, commonly used among fire workers, had two valves that separated incoming and exhaled airflow. The flow of both cylinders could be adjusted to create a part with compressed normal air and a part with a compressed air mixture with 5% CO₂.
**Self-reported symptoms**

The symptoms breathlessness, dizziness, nausea, heart pounding, tenseness, and anxiety were selected as symptoms that will most likely be experienced as a result of CO₂-enriched air inhalation (see Van den Bergh, et al., 1997). These symptoms were measured (repeatedly) on seven-point scales, ranging from 1 ‘not at all’ to 7 ‘very much’. The words were presented on the computer screen, and participants had to rate the degree they experienced the presented symptom (at that moment) and they had to type the corresponding number on the keyboard. The scores for breathlessness, dizziness, nausea, and heart pounding were pooled and named ‘somatic symptoms’, the scores for tenseness and anxiety were pooled and named ‘tenseness-anxiety’.

**Physiological recordings**

Inter Beat Intervals (IBI’s), systolic time intervals, respiratory rate, and a raw estimate of changes in respiratory depth (tidal volume) were measured with the Vrije Universiteit Ambulatory Monitoring System (VU-AMS version 4.3, TD-FPP, Vrije Universiteit, Amsterdam, The Netherlands). This device uses six Ag/AgCl electrodes to record the electrocardiogram and thoracic impedance (dZ). Details on the measurement procedure with the VU-AMS can be found in de Geus, Willemsen, Klaver, and van Doornen (1995) and Willemsen, de Geus, Klaver, van Doornen, and Carroll (1996).

The PaCO₂ was estimated by measuring the partial pressure of CO₂ in the exhaled air at the end of a normal expiration (PetCO₂). This was measured with the Capnogard etCO₂ Monitor (Novametrix, Walingford, CT, USA) and expressed in mm/Hg. A small tube was inserted in each of the participants’ nostrils. The values were automatically fed into a separate MS-DOS computer that was connected to the main system for synchronization of measuring intervals.

**Physiological data analysis**

The heart period data of each participant were analyzed in segments representing 128 seconds. An artifact pre-processing was performed on the IBI data by detecting outlier IBI values with three methods: (a) by absolute values (>1800 ms or <300 ms), (b) a moving average filter (> 3 SD deviation from the moving mean), and (c) by visual inspection. Since artifacts cannot simply be deleted because the continuity of time would be lost, spuriously short IBI’s were summed and missing beats were ‘created’ by splitting spuriously long IBI’s. The IBI mean values were computed from these corrected data. Next, uniformly spaced samples were created, and the segments were discrete Fourier transformed. Heart period power values were computed for the High Frequency (HF) band (0.125 - 0.5 Hz). Changes in these HF power values were used to estimate changes in RSA. The power values were log₁₀ transformed to obtain normal distributions.
Chapter 6

The thoracic impedance (dZ) data (sampled at 10 Hz) were band-pass filtered by a discrete wavelet transform filter with a cubic spline function as base (0.125 - 0.5 Hz). Next, the respiratory power values were computed from this filtered thoracic impedance (dZ) data by computing the variance of this filtered time series. Changes in the respiratory power values were used as a (raw) estimation of changes in respiratory depth (tidal volume). The respiratory power values were also log\textsuperscript{10} transformed to obtain normal distributions. The mean respiratory rate values were estimated from the band pass filtered thoracic impedance (dZ) data by counting the number of up-going zero crossings and dividing this value by the time of a segment. This procedure is comparable to the method used by de Geus and co-workers (1995) who computed the mean total respiratory cycle time as the mean interval between the initiating moments of inspiration.

The dZ/dt values (sampled at 250 Hz around each R-wave) were ensemble averaged over 60 seconds. The B-points were manually determined for each ensemble averaged segment, and the PEP values were determined by summing a fixed Q-to-R interval of 48 ms to the R-B interval time. The 1 minute ensemble averaged PEP’s were pooled over two succeeding values to obtain a value for each 2 minute period, similar to the other measures.

**Statistical data analysis**

For each measure, nine repeated observations were available for each participant (three conditions with three different breathing parts of 4 minutes). Base-rate differences between the groups were tested for the relaxation condition during normal breathing (i.e., the conditions without breathing through the face mask). Next, within-subject effects of condition and breathing manipulation and interactions with group were tested with repeated measures MANOVA tests using Wilks’ Lambda. The alpha level was set at the .05 level for all statistical tests.

**Results**

**Participants**

No significant group differences were found for age, length, and weight (see Table 1), smoking behavior ($\chi^2(1)=0.44, p=.50$), sporting behavior ($\chi^2(1)=1.08, p=.30$), and the use of oral contraceptives ($\chi^2(1)=0.13, p=.72$). However, participants of the HSS group scored (as expected) significantly higher on the HSQ ($T(34)=10.65, p<.001$), but they also scored significantly higher on the STAI ($T(34)=6.91, p<.001$). A significant and high correlation was found between the HSQ and STAI scores ($r=.86, n=36, p<.001$).
Table 1. Group mean (and SD) values for age, length, weight, HSQ and STAI scores.

<table>
<thead>
<tr>
<th></th>
<th>LSS M (SD)</th>
<th>HSS M (SD)</th>
<th>sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>20.61 (2.43)</td>
<td>19.78 (1.22)</td>
<td>NS</td>
</tr>
<tr>
<td>Length</td>
<td>170.50 (6.48)</td>
<td>174.17 (6.11)</td>
<td>NS</td>
</tr>
<tr>
<td>Weight</td>
<td>63.50 (6.93)</td>
<td>64.78 (8.54)</td>
<td>NS</td>
</tr>
<tr>
<td>HSQ</td>
<td>7.61 (4.15)</td>
<td>33.28 (9.35)</td>
<td>***</td>
</tr>
<tr>
<td>STAI</td>
<td>31.17 (5.06)</td>
<td>48.94 (9.68)</td>
<td>***</td>
</tr>
</tbody>
</table>

Notes: LSS=low in somatic symptoms; HSS=high in somatic symptoms

***p<.001 (2-tailed)

Self-reported symptoms

See Table 2 for mean values of self-reported base-rate scores (i.e., for the relaxation condition during normal breathing) and mean values of within-subject change scores with these base-rate values.

Condition and breathing manipulation. A significant condition effect was found for somatic symptoms ($F(2,33)=40.22$, $p<.001$) and tenseness-anxiety ($F(2,33)=31.73$, $p<.001$). Follow-up tests revealed significantly increased somatic symptoms and tenseness-anxiety during mental stress as compared to relaxation ($F_{som-sym}(1,34)=77.35$, $p<.001$; $F_{ten-anx}(1,34)=64.83$, $p<.001$), increased somatic symptoms during exercise as compared to relaxation ($F(1,34)=17.43$, $p<.001$), and increased somatic symptoms and tenseness-anxiety during mental stress as compared to exercise ($F_{som-sym}(1,34)=18.17$, $p<.001$; $F_{ten-anx}(1,34)=54.47$, $p<.001$). A significant breathing manipulation effect was found for somatic symptoms ($F(2,33)=50.05$, $p<.001$) and tenseness-anxiety ($F(2,33)=17.72$, $p<.001$). Follow-up tests revealed significantly increased somatic symptoms during compressed normal air breathing as compared to normal breathing ($F(1,34)=21.25$, $p<.001$), increased somatic symptoms and tenseness-anxiety during compressed 5% CO$_2$-enriched air breathing as compared to normal breathing ($F_{som-sym}(1,34)=103.04$, $p<.001$; $F_{ten-anx}(1,34)=35.25$, $p<.001$), and increased somatic symptoms and tenseness-anxiety during compressed 5% CO$_2$-enriched air breathing as compared to compressed normal air breathing ($F_{som-sym}(1,34)=86.42$, $p<.001$; $F_{ten-anx}(1,34)=35.17$, $p<.001$).

Group differences. The HSS participants reported, as expected, significantly more base-rate somatic symptoms ($T(17.45)=3.08$, $p<.01$) and tenseness-anxiety ($T(18.24)=2.88$, $p<.01$). A significant condition by group interaction was found for somatic symptoms ($F(2,33)=4.92$, $p<.05$) and tenseness-anxiety ($F(2,33)=3.49$, $p<.05$).
Follow-up tests revealed that the HSS participants reported significantly more somatic symptoms and tenseness-anxiety than LSS participants during mental stress as compared to relaxation ($F_{som-sym}(1,34)=10.11$, $p<.01$; $F_{ten-anx}(1,34)=7.12$, $p<.01$), and they reported significantly more somatic symptoms and tenseness-anxiety during mental stress as compared to exercise ($F_{som-sym}(1,34)=4.19$, $p<.05$; $F_{ten-anx}(1,34)=5.98$, $p<.05$). A significant breathing manipulation by group interaction was found for somatic symptoms ($F(2,33)=5.89$, $p<.01$). Follow-up tests revealed that HSS participants reported significantly more somatic symptoms than LSS participants during compressed normal air breathing as compared to normal breathing ($F(1,34)=8.27$, $p<.01$), they reported more somatic symptoms during compressed 5% CO$_2$-enriched air breathing as compared to normal breathing ($F(1,34)=9.67$, $p<.01$), and they reported more somatic symptoms during compressed 5% CO$_2$-enriched air breathing as compared to compressed normal air breathing ($F(1,34)=4.53$, $p<.05$).

### Table 2. Group mean (and SD) values for self-reported base-rate values and within-subject change scores with these base-rate values.

<table>
<thead>
<tr>
<th>Condition</th>
<th>LSS M (SD)</th>
<th>HSS M (SD)</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-rate</td>
<td>somatic symptoms</td>
<td>tension-anxiety</td>
<td></td>
</tr>
<tr>
<td>Stress no mask</td>
<td>1.03 (0.00)</td>
<td>1.54 (0.92)</td>
<td>**</td>
</tr>
<tr>
<td>Stress normal air</td>
<td>0.40 (0.43)</td>
<td>1.17 (0.83)</td>
<td>**</td>
</tr>
<tr>
<td>Stress 5% CO$_2$</td>
<td>0.39 (0.43)</td>
<td>1.28 (0.97)</td>
<td>**</td>
</tr>
<tr>
<td>Relaxation normal air</td>
<td>1.28 (0.95)</td>
<td>2.50 (1.23)</td>
<td>**</td>
</tr>
<tr>
<td>Relaxation 5% CO$_2$</td>
<td>0.06 (0.16)</td>
<td>0.54 (0.71)</td>
<td>*</td>
</tr>
<tr>
<td>Exercise no mask</td>
<td>0.65 (0.65)</td>
<td>1.50 (1.02)</td>
<td>**</td>
</tr>
<tr>
<td>Exercise normal air</td>
<td>0.08 (0.19)</td>
<td>0.26 (0.74)</td>
<td>NS</td>
</tr>
<tr>
<td>Exercise 5% CO$_2$</td>
<td>0.31 (0.45)</td>
<td>0.75 (0.87)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Notes: LSS=low in somatic symptoms; HSS=high in somatic symptoms

* $p<.05$  ** $p<.01$ (2-tailed)

$^a$ the relaxation, no mask condition is used as base-rate.
### Table 3. Group mean (and SD) values for physiological base-rate values and within-subject change scores with these base-rate values.

<table>
<thead>
<tr>
<th></th>
<th>LSS M (SD)</th>
<th>HSS M (SD)</th>
<th>Sign.</th>
<th>LSS M (SD)</th>
<th>HSS M (SD)</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>log&lt;sup&gt;10&lt;/sup&gt; HF power</td>
<td></td>
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</tr>
<tr>
<td>base-rate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.23 (0.39)</td>
<td>3.32 (0.34)</td>
<td>NS</td>
<td>0.25 (0.04)</td>
<td>0.24 (0.04)</td>
<td>NS</td>
</tr>
<tr>
<td>stress no mask</td>
<td>-0.33 (0.33)</td>
<td>-0.41 (0.26)</td>
<td>NS</td>
<td>0.03 (0.07)</td>
<td>0.04 (0.08)</td>
<td>NS</td>
</tr>
<tr>
<td>stress normal air</td>
<td>-0.30 (0.34)</td>
<td>-0.35 (0.27)</td>
<td>NS</td>
<td>0.02 (0.06)</td>
<td>0.03 (0.05)</td>
<td>NS</td>
</tr>
<tr>
<td>stress 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>0.02 (0.32)</td>
<td>-0.16 (0.42)</td>
<td>NS</td>
<td>0.03 (0.05)</td>
<td>0.05 (0.06)</td>
<td>NS</td>
</tr>
<tr>
<td>relaxation normal air</td>
<td>0.05 (0.16)</td>
<td>0.04 (0.26)</td>
<td>NS</td>
<td>-0.00 (0.03)</td>
<td>-0.01 (0.03)</td>
<td>NS</td>
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<tr>
<td>relaxation 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>0.25 (0.26)</td>
<td>0.23 (0.27)</td>
<td>NS</td>
<td>0.02 (0.05)</td>
<td>0.03 (0.04)</td>
<td>NS</td>
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<tr>
<td>exercise no mask</td>
<td>-0.56 (0.34)</td>
<td>-0.73 (0.38)</td>
<td>NS</td>
<td>0.08 (0.06)</td>
<td>0.07 (0.04)</td>
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<tr>
<td>exercise normal air</td>
<td>-0.42 (0.40)</td>
<td>-0.52 (0.37)</td>
<td>NS</td>
<td>0.04 (0.05)</td>
<td>0.04 (0.05)</td>
<td>NS</td>
</tr>
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<td>exercise 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-0.15 (0.44)</td>
<td>-0.43 (0.46)</td>
<td>NS</td>
<td>0.04 (0.04)</td>
<td>0.06 (0.06)</td>
<td>NS</td>
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<tr>
<td>IBI (sec)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>base-rate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.91 (0.15)</td>
<td>0.92 (0.11)</td>
<td>NS</td>
<td>0.62 (0.27)</td>
<td>0.52 (0.28)</td>
<td>NS</td>
</tr>
<tr>
<td>stress no mask</td>
<td>-0.19 (0.08)</td>
<td>-0.19 (0.11)</td>
<td>NS</td>
<td>0.13 (0.32)</td>
<td>0.19 (0.28)</td>
<td>NS</td>
</tr>
<tr>
<td>stress normal air</td>
<td>-0.19 (0.08)</td>
<td>-0.19 (0.11)</td>
<td>NS</td>
<td>0.21 (0.34)</td>
<td>0.14 (0.27)</td>
<td>NS</td>
</tr>
<tr>
<td>stress 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-0.02 (0.02)</td>
<td>-0.20 (0.12)</td>
<td>NS</td>
<td>0.64 (0.33)</td>
<td>0.63 (0.33)</td>
<td>NS</td>
</tr>
<tr>
<td>relaxation normal air</td>
<td>-0.09 (0.05)</td>
<td>-0.08 (0.07)</td>
<td>NS</td>
<td>0.11 (0.19)</td>
<td>0.06 (0.13)</td>
<td>NS</td>
</tr>
<tr>
<td>relaxation 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-0.20 (0.08)</td>
<td>-0.20 (0.10)</td>
<td>NS</td>
<td>0.18 (0.25)</td>
<td>0.24 (0.19)</td>
<td>NS</td>
</tr>
<tr>
<td>exercise no mask</td>
<td>-0.21 (0.07)</td>
<td>-0.22 (0.10)</td>
<td>NS</td>
<td>0.48 (0.31)</td>
<td>0.42 (0.21)</td>
<td>NS</td>
</tr>
<tr>
<td>exercise normal air</td>
<td>-0.23 (0.08)</td>
<td>-0.24 (0.11)</td>
<td>NS</td>
<td>0.87 (0.35)</td>
<td>0.80 (0.25)</td>
<td>NS</td>
</tr>
<tr>
<td>PEP (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>base-rate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>91.20 (9.03)</td>
<td>87.06 (4.67)</td>
<td>NS</td>
<td>36.90 (2.38)</td>
<td>36.47 (1.93)</td>
<td>NS</td>
</tr>
<tr>
<td>stress no mask</td>
<td>-7.71 (7.65)</td>
<td>-2.96 (2.51)</td>
<td>*</td>
<td>-0.68 (2.03)</td>
<td>-0.20 (0.96)</td>
<td>NS</td>
</tr>
<tr>
<td>stress normal air</td>
<td>-8.24 (7.73)</td>
<td>-2.52 (2.95)</td>
<td>**</td>
<td>0.14 (1.19)</td>
<td>0.57 (1.03)</td>
<td>NS</td>
</tr>
<tr>
<td>stress 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-8.02 (7.22)</td>
<td>-2.78 (2.39)</td>
<td>**</td>
<td>8.28 (1.62)</td>
<td>7.84 (1.97)</td>
<td>NS</td>
</tr>
<tr>
<td>relaxation normal air</td>
<td>0.31 (2.39)</td>
<td>1.20 (2.40)</td>
<td>NS</td>
<td>0.40 (0.66)</td>
<td>0.13 (1.51)</td>
<td>NS</td>
</tr>
<tr>
<td>relaxation 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-0.45 (3.17)</td>
<td>-0.22 (2.41)</td>
<td>NS</td>
<td>8.06 (1.79)</td>
<td>8.46 (1.59)</td>
<td>NS</td>
</tr>
<tr>
<td>exercise no mask</td>
<td>-6.29 (6.69)</td>
<td>-2.39 (3.42)</td>
<td>*</td>
<td>1.30 (0.99)</td>
<td>1.80 (1.13)</td>
<td>NS</td>
</tr>
<tr>
<td>exercise normal air</td>
<td>-7.41 (7.51)</td>
<td>-2.63 (3.56)</td>
<td>*</td>
<td>3.54 (2.16)</td>
<td>3.32 (1.63)</td>
<td>NS</td>
</tr>
<tr>
<td>exercise 5% CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-8.96 (8.02)</td>
<td>-3.35 (3.56)</td>
<td>*</td>
<td>12.07 (2.41)</td>
<td>11.05 (2.45)</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Notes:** LSS=low in somatic symptoms; HSS=high in somatic symptoms
*<sup>p</sup><.05  **<sup>p</sup><.01  ***<sup>p</sup><.001  (2-tailed)
<sup>a</sup>the relaxation, no mask condition is used as base-rate.

**Physiological measures**

See Table 3 for mean values of physiological base-rate values (i.e., for the relaxation condition during normal breathing) and mean values of within-subject change scores with these base-rate values.
Chapter 6

Condition and breathing manipulation. A significant condition effect was found for IBI \((F(2,32)=134.03, p<.001)\), PEP \((F(2,32)=20.12, p<.001)\), HF heart period variability power \((F(2,31)=50.02, p<.001)\), respiratory rate \((F(2,31)=33.38, p<.001)\), respiratory power \((F(2,31)=30.57, p<.001)\), and PetCO\(_2\) \((F(2,32)=55.64, p<.001)\). Follow-up tests revealed significantly reduced IBI, PEP, and HF heart period variability power values but increased respiratory rate during mental stress as compared to relaxation \((F_{\text{IBI}}(1,33)=129.04, p<.001; F_{\text{PEP}}(1,33)=40.17, p<.001; F_{\text{HFpower}}(1,33)=58.79, p<.001; F_{\text{RR}}(1,33)=10.53, p<.01)\), reduced IBI, PEP, and HF heart period variability power values but increased respiratory rate, respiratory power, and PetCO\(_2\) during exercise as compared to relaxation \((F_{\text{IBI}}(1,33)=200.67, p<.001; F_{\text{PEP}}(1,33)=31.50, p<.001; F_{\text{HFpower}}(1,33)=102.82, p<.001; F_{\text{RR}}(1,33)=66.85, p<.001; F_{\text{Rpower}}(1,33)=51.16, p<.001; F_{\text{PetCO}_2}(1,33)=105.77, p<.001)\), and reduced IBI and HF heart period variability power values but increased respiratory rate, respiratory power, and PetCO\(_2\) during exercise as compared to mental stress \((F_{\text{IBI}}(1,33)=56.38, p<.001; F_{\text{HFpower}}(1,33)=41.06, p<.001; F_{\text{RR}}(1,33)=12.06, p<.001; F_{\text{Rpower}}(1,33)=23.46, p<.001; F_{\text{PetCO}_2}(1,33)=91.07, p<.001)\).

A significant breathing manipulation effect was found for IBI \((F(2,32)=13.75, p<.001)\), HF heart period variability power \((F(2,31)=30.71, p<.001)\), respiratory rate \((F(2,31)=12.45, p<.001)\), respiratory power \((F(2,31)=173.14, p<.001)\), and PetCO\(_2\) \((F(2,32)=734.37, p<.001)\). Follow-up tests revealed significantly reduced IBI values and respiratory rate, but increased HF heart period variability power, respiratory power, and PetCO\(_2\) during compressed normal air breathing as compared to normal breathing \((F_{\text{IBI}}(1,33)=6.01, p<.05; F_{\text{HFpower}}(1,33)=13.30, p<.001; F_{\text{RR}}(1,33)=16.31, p<.001; F_{\text{Rpower}}(1,33)=39.06, p<.001; F_{\text{PetCO}_2}(1,33)=49.44, p<.001)\), reduced IBI values but increased HF heart period variability power, respiratory power, and PetCO\(_2\) during compressed 5% CO\(_2\)-enriched air breathing as compared to normal breathing \((F_{\text{IBI}}(1,33)=27.14, p<.001; F_{\text{HFpower}}(1,33)=62.64, p<.001; F_{\text{Rpower}}(1,33)=39.38, p<.001; F_{\text{PetCO}_2}(1,33)=1262.53, p<.001)\), and reduced IBI values and respiratory rate but increased HF heart period variability power, respiratory power, and PetCO\(_2\) during compressed 5% CO\(_2\)-enriched air breathing as compared to compressed normal air breathing \((F_{\text{IBI}}(1,33)=13.82, p<.01; F_{\text{HFpower}}(1,33)=31.53, p<.001; F_{\text{RR}}(1,33)=14.15, p<.001; F_{\text{Rpower}}(1,33)=308.36, p<.001; F_{\text{PetCO}_2}(1,33)=1473.44, p<.001)\).

Group differences. The groups did not differ significantly on any of the physiological base-rate values, and no interaction effects between group and breathing manipulation were found. However, one significant interaction between group and condition was found for PEP (see Figure 1; \(F(2,32)=3.82, p<.05\)). Follow-up tests revealed that HSS participants had significantly less PEP reduction than LSS participants during mental stress as compared to relaxation \((F(1,33)=7.81, p<.01)\), and they had less PEP reduction during exercise as compared to relaxation \((F(1,33)=5.38, p<.05)\).
Participants with numerous functional somatic symptoms showed the expected higher base-rates in self-reported somatic symptoms and anxiety-tenseness, and these group differences sharply increased during mental stress, exercise, and during 5% CO₂-enriched air breathing. However, high levels of functional somatic symptoms were not related to reduced base-rate RSA values or to larger task-related RSA reductions. Additionally, participants with numerous functional somatic symptoms did not show relatively lower RSA-values in response to inhaling the CO₂-enriched air mixture during any of the tasks. Finally, the groups did not show differences on PetCO₂, heart rate, tidal volume, or respiratory rate. The results of the current study, therefore, clearly indicate that functional somatic symptoms suggestive of hyperventilation could not be associated with a disruption in the RSA regulatory system.

It should be noted that the participants with numerous functional somatic symptoms were not selected from a clinical population. Nonetheless, they reported high scores on the used hyperventilation symptom questionnaire, similar to the

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**Discussion**

Participants with numerous functional somatic symptoms showed the expected higher base-rates in self-reported somatic symptoms and anxiety-tenseness, and these group differences sharply increased during mental stress, exercise, and during 5% CO₂-enriched air breathing. However, high levels of functional somatic symptoms were not related to reduced base-rate RSA values or to larger task-related RSA reductions. Additionally, participants with numerous functional somatic symptoms did not show relatively lower RSA-values in response to inhaling the CO₂-enriched air mixture during any of the tasks. Finally, the groups did not show differences on PetCO₂, heart rate, tidal volume, or respiratory rate. The results of the current study, therefore, clearly indicate that functional somatic symptoms suggestive of hyperventilation could not be associated with a disruption in the RSA regulatory system.

It should be noted that the participants with numerous functional somatic symptoms were not selected from a clinical population. Nonetheless, they reported high scores on the used hyperventilation symptom questionnaire, similar to the
scores of the patients measured by Hornsveld and co-workers (1996). They also reported high scores on trait anxiety, and they experienced pronounced increased somatic symptoms during the tasks and air mixture manipulations of the current study. Thus, although the results of this study do not exclude the possibility that a clinical population may show reduced RSA values (as found by Thayer et al., 1996; Watkins et al., 1998), it does demonstrate that reduced RSA values may not (generally) be related to functional somatic symptoms.

The expected relation was found between somatic symptoms and tenseness-anxiety scores. Because functional somatic symptoms are closely tied to anxiety and/or psychological distress (Watson & Pennebaker, 1989; Pennebaker, 1982; Wientjes & Grossman, 1994), a possible explanation may be found in an anxiety-related lowered threshold for detection of physical symptoms in individuals with numerous functional somatic symptoms. There is evidence that highly anxious individuals attend more to bodily symptoms, and that attention to bodily symptoms increases the perceived intensity of these symptoms (Pennebaker, 1982; Pennebaker & Skelton, 1978; Pennebaker & Lightner, 1980). Thus, the increased self-reported anxiety and tenseness of the participants with numerous functional somatic symptoms could have resulted in increased functional somatic symptoms as a result of this psychological mechanism.

A reduced PEP reactivity was found for participants with numerous functional somatic symptoms compared to the control group. This difference might indicate a difference between the groups in beta-adrenergic influence on the heart (Sherwood et al., 1990; Bum-Hee, Dimsdale, & Mills, 1999), indicating that participants with numerous functional somatic symptoms have reduced beta-adrenergic reactivity. Bum-Hee and co-workers (1999) demonstrated that tension-anxiety ratings (measured by the ‘profile of mood states’) are negatively correlated with beta-adrenergic receptor density, even in participants who do not have psychiatric illness. However, another explanation for the observed reduced PEP reactivity for participants with numerous functional somatic symptoms may be an increased tendency to respond to stress with increases in peripheral vascular resistance. Manuck, Kamarck, Kasprowicz, and Waldstein (1993) identified stable individual differences in cardiovascular reactivity in response to psychological stress caused by a mental arithmetic task. Cardiac output (i.e., the product of heart rate and stroke volume) reactors were identified based on a relatively high rise in cardiac output and relatively high PEP reactivity, while peripheral vascular resistance reactors were identified based on a relatively high rise in peripheral vascular resistance and relatively low PEP reactivity. The correlation between peripheral vascular resistance and PEP reactivity reflects an effect of an increased afterload that lengthens PEP, and may thus mask a true increase in cardiac sympathetic drive (Sherwood and co-workers, 1990). Therefore, our PEP results may not have signaled lower sympathetic reactivity for participants with functional somatic symptoms, but increased peripheral vascular resistance reactivity and/or lowered cardiac output reactivity. Since no blood pressure was
measured, this question could not be properly resolved and deserves future attention.

The results of the current study indicate that reduced RSA values are not (generally) related to functional somatic symptoms. RSA still may have its effect on the regulation of arterial partial pressure of O₂. However, the results also indicate that a dysregulation in the arterial partial pressure of O₂, as a result of a impaired cardiorespiratory coupling, can not (generally) be related to functional somatic symptoms.

Acknowledgments

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References


