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Behaviour Research and Therapy ∎ (∎∎∎∎) ∎∎∎–∎∎∎

BEHAVIOUR RESEARCH AND THERAPY

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# Hyperventilation in patients with chronic fatigue syndrome: The role of coping strategies

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Received 19 April 2007; received in revised form 8 July 2007; accepted 16 July 2007

**Abstract**

Hyperventilation has been suggested as a concomitant and possible maintaining factor that may contribute to the symptom pattern of chronic fatigue syndrome (CFS). Because patients accepting the illness and trying to live with it seem to have a better prognosis than patients chronically fighting it, we investigated breathing behavior during different coping response sets towards the illness in patients with CFS ($N = 30$, CDC criteria). Patients imagined a relaxation script (baseline), a script describing a coping response of hostile resistance, and a script depicting acceptance of the illness and its (future) consequences. During each imagery trial, end-tidal $PCO_2$ (Handheld Capnograph, Oridion) was measured. After each trial, patients filled out a symptom checklist. Results showed low resting values of $PetCO_2$ overall, while only imagery of hostile resistance triggered a decrease and deficient recovery of $PetCO_2$. Also, more hyperventilation complaints and complaints of other origin were reported during hostile resistance imagery compared with acceptance and relaxation. In conclusion, hostile resistance seems to trigger both physiological and symptom perception processes contributing to the clinical picture of CFS.


*Keywords:* Hyperventilation; Chronic fatigue syndrome; Imagery; Coping; Acceptance; Interoception

## Introduction

The chronic fatigue syndrome (CFS) is a condition characterized by persistent medically unexplained fatigue, lasting for at least 6 months, the co-occurrence of several other unexplained symptoms, and severe functional disability (Fukuda et al., 1994).

Hyperventilation is defined as a breathing pattern in excess of metabolic needs (Gardner, 1996). Because more $CO_2$ is being exhaled than is produced by the body, arterial partial $CO_2$ pressure decreases. This state of

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0005-7967/$ - see front matter 
doi:10.1016/j.brat.2007.07.003

Please cite this article as: Bogaerts, K., et al. Hyperventilation in patients with chronic fatigue syndrome: The role of coping strategies. *Behaviour Research and Therapy* (2007), doi:10.1016/j.brat.2007.07.003

hypocapnia induces an increased blood pH and causes a wide range of bodily symptoms, largely overlapping with those characterizing CFS (e.g. fatigue, feeling of exertion, muscle pain, sore throat, headache, loss of concentration, etc.). This overlap has led researchers to consider the role of hyperventilation in CFS. Yet, the literature on this topic is limited and inconsistent. Some researchers believe that hyperventilation is an epiphenomenon of CFS (Bazelmans, Bleijenberg, Vercoulen, van der Meer, & Folgering, 1997; Riley, O'Brien, McCluskey, Bell, & Nicholls, 1990; Saisch, Deale, Gardner, & Wessely, 1994; Tweeddale, Rowbottom, & McHardy, 1994), whereas others conceive of it as an important perpetuating factor (Neerinckx, Lysens, Van Houdenhove, & Vertommen, 1999) or even as an etiological factor (Rosen, King, Wilkinson, & Nixon, 1990; for discussion, see Lavietes, Natelson, Cordero, Ellis, & Tapp, 1996). Due to methodological differences, direct comparisons across studies are difficult, but the best conclusion seems that hyperventilation occurs in some CFS patients under some circumstances. The important question, therefore, is which type of patient hyperventilates in which type of situation.

The tendency to hyperventilate typically occurs during action tendencies characterized by high arousal (Van Diest et al., 2001), suggesting that specifically CFS patients who anticipate a distressing and demanding activity may be vulnerable to disproportionate breathing. Therefore, hyperventilation in CFS patients may only show up in contexts evoking emotions relevant to them and may not appear as a stable characteristic of patients across situations. This perspective may explain the difference between literature suggesting a limited or non-existing role for hyperventilation in CFS (Bazelmans et al., 1997; Riley et al., 1990; Saisch et al., 1994; Tweeddale et al., 1994) and the study of Neerinckx et al. (1999). Whereas the former studies registered breathing behavior within an emotionally neutral context, the patients in the study of Neerinckx were preparing for a demanding exercise test. Hyperventilation was observed in 45% of the patients. Hence, hyperventilation is not likely to be a causal factor for CFS, but it might be an important perpetuating factor for some of the patients.

It is known that strategies to cope with a chronic disease may influence the clinical picture and ultimately the course of the illness. For example, studies on chronic pain have demonstrated a positive relationship between acceptance of the disease and lower subjective pain intensity, less anxiety/depression, less avoidance of activity, less impairment, more engagement with daily activities, less attention to pain, fewer health-care visits for pain, and less medication consumption (McCracken, 1998; McCracken & Eccleston, 2005; Viane et al., 2003; Viane, Crombez, Eccleston, Devulder, & De Corte, 2004).

Research on the role of acceptance in CFS is at an early but promising stage. For example, Van Damme, Crombez, Van Houdenhove, Mariman, and Michielsen (2006) showed that acceptance was associated with better quality of life in a CFS population, whereas it was negatively correlated with fatigue, functional disability, and psychological problems. In the present study, we used an imagery paradigm to compare the breathing behavior during two different action sets, namely acceptance vs. hostile resistance, towards the illness in CFS patients. Script-driven imagery is considered a valid and generally accepted tool to elicit emotions both in psychophysiological studies (Lang, 1979; Van Diest et al., 2001) and in PET studies on the neuroanatomy of emotions (Dougherty et al., 1999; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997). In accordance with definitions in the area of pain, we defined acceptance of chronic fatigue as a willingness to live with fatigue without reactance, disapproval, or attempts to reduce or avoid it. Accepting CFS means giving up the battle against the illness along with unproductive attempts to control it, adopting a realistic approach towards the illness, learning to live with it without losing engagement in positive everyday activities, and not letting oneself be reduced to the patient's status (Hayes, Jacobson, Follette, & Dougher, 1994; Risdon, Eccleston, Crombez, & McCracken, 2003). Conversely, hostile resisting was defined as fighting the illness and undertaking incessant attempts to control it. Resisting patients want to become as healthy and energetic as before, have difficulties with the chronic character of the disease, and do not want to make any concession. Because the latter strategy is more likely associated with the mobilization of action tendencies, we expected to observe the tendency to hyperventilate particularly in the mental set of hostile resistance towards one's own illness.

We also explored the role of worrying, as it is a maladaptive coping strategy, implying attentional vigilance and exaggerated inference of threat (MacLeod & Rutherford, 2004). Worrying has been defined as repetitive thought activity, characterized by an automatic, negative, and unrealistic interpretation of feared future events. Excessive worry produces negative emotional states (Borkovec, Ray, & Stöber, 1998) and is associated with increased pain reporting (Keefe et al., 2001) and self-reported illness symptoms (Brosschot & van der Doef, 2006).

In the current study, each patient was presented auditorily with four scripts (neutral, relaxation, hostile resistance, and acceptance), which she had to imagine as vividly as possible. End-tidal $PCO_2$ was measured continuously during imagery and subjective symptoms were rated after each trial. Hyperventilation was operationalized as a statistically significant decrease in $P$et$CO_2$ from baseline to imagery. We hypothesized that imagery of the hostile resistance script (1) would cause a statistically significant decrease in $P$et$CO_2$ from baseline to imagery and (2) would produce more hyperventilation complaints than imagery of the acceptance and relaxation script.

## Methods

### *Participants*

Thirty female participants (21–54 years) were recruited through a systematic multidisciplinary screening of CFS patients at the general internal medicine clinic of the university hospital. Patients underwent an extensive somatic investigation, effort capacity measurements, and a psychiatric in-depth interview. All patients met CDC criteria for CFS (Fukuda et al., 1994). Patients with an underlying organic disease or a psychiatric condition as possible explanation of their fatigue were excluded from the sample, as well as CFS patients with comorbid anxiety disorders. The study was approved by the local medical ethics committee and all participants provided written informed consent.

### *Scripts*

Four scripts were used (Appendix). The neutral script was always presented first, to familiarize the patients with the instructions and the procedure of the experiment. Next, the patients imagined a relaxation script (R), a script describing an action set of hostile resistance (HR), and a script describing an action set of acceptance of the illness and its consequences (ACC) in randomized order. We created two versions of the HR and ACC scripts: one version described the patient having unexpected visitors and the other version described the patient waiting in line at a grocery store. Versions were counterbalanced across patients: patients who imagined the visit-version for the HR script, imagined the store-version for the ACC script and vice versa.

The neutral script and the relaxation script have previously been used by our group (Van Diest et al., 2001). The scenarios for the hostile resistance and acceptance scripts were based on pilot interviews and clinical observations and were judged as recognizable and familiar by all CFS patients. No wordings referring to respiratory behavior were used to avoid response-specific demand effects.

### *Subjective measures*

#### *Positive and Negative Affect Schedule (PANAS)*

The Dutch state version of the PANAS consists of 10 positive (positive affectivity; PA) and 10 negative adjectives (negative affectivity; NA). Participants indicate on a 5-point scale the extent to which the items apply to his/her feeling right now. The reliability and construct validity of the PANAS have been documented (Engelen, De Peuter, Victoir, Van Diest, & Van den Bergh, 2006; Watson, Clark, & Tellegen, 1988).

#### *Symptom checklist*

Subjective complaints were assessed by the checklist for psychosomatic symptoms (Wientjes & Grossman, 1994; 39 items). This questionnaire is an extension of the Nijmegen Questionnaire (16 items; van Dixhoorn & Duivenvoorden, 1985), which tests hyperventilation. Other symptoms were added to measure a variety of other symptoms that frequently occur in psychosomatic patients (see Wientjes & Grossman, 1994, and Han, Schepers, Stegen, Van den Bergh, & Van de Woestijne, 2000 for components and reliability). For each symptom, a 5-point graded intensity response (not at all, a little bit, quite, rather strongly, very strongly) was required to the question “To what extent do (did) you experience the following symptoms at this moment (during the past imagery trial)?''. Two subscores were calculated and analyzed separately: (a) hyperventilation complaints and (b) additional complaints. The hyperventilation subscore was the sum of 14 items: feeling tense, dizziness, faster or deeper breathing, shortness of breath, discomfort in or around the chest, palpitations, anxious feeling, unable to breathe deeply, confusion or feeling of losing contact with surroundings, bloated abdomen, tingling fingers, chest pain, stiff fingers or arms, and cold hands or feet. These 14 items are the core of the Nijmegen Questionnaire and are considered prototypical symptoms of hyperventilation. The remaining symptoms (25 items) were totalled to form a subset of additional complaints. These symptoms were considered atypical for hyperventilation. Examples are stuffed nose, feeling sleepy, low back pain, headache, and burning eyes.

*Acceptance Chronic Fatigue Test (ACFT)*

The ACFT is the Dutch version of the Chronic Pain Acceptance Questionnaire (CPAQ), adapted for chronic fatigue (Crombez, Van Houdenhove, Mariman, & Michielsen, 2002). Participants indicate on a 6-point scale to what extent 24 statements are applicable to themselves. Following the scoring procedure of Geiser (1992) a single total score is calculated (with higher scores reflecting higher levels of acceptance). The original CPAQ (34 items) is a reliable measure of the tendency to accept chronic pain (Geiser, 1992). The present questionnaire has not been validated for CFS. Data from this measure are presented for exploratory purposes.

*Penn-State Worry Questionnaire (PSWQ)*

The PSWQ is comprised of 16 items measuring the trait-like tendency to worry. Participants indicate on a 5-point scale the extent to which the items characterize them (1 = not at all to 5 = very characteristic). Higher scores reflect higher levels of worry. The PSWQ has a high internal consistency, high test–retest reliability, as well as favorable convergent and discriminant validity (Meyer, Miller, Metzger, & Borkovec, 1990). We used the Dutch version of the PSWQ, which has been shown to be reliable and valid (van Rijsoort, Emmelkamp, & Vervaeke, 1999).

*Self-assessment Manikin*

Experiences during the imagery trials were judged on the affective dimensions of valence, arousal, and dominance (Lang, Bradley, & Cuthbert, 1990; Mehrabian & Russell, 1974), using a paper-and-pencil version of the 9-point Manikin rating system (Bradley & Lang, 1994). In this system, values along each of the three dimensions are portrayed on a continuous scale in a non-verbal, pictorial way. For the valence dimension, values range from a smiling, happy figure to a frowning, unhappy figure. The arousal dimension ranges from an excited, wide-eyed figure to a relaxed, sleepy figure. The scale ranges from a small figure (dominated) to a large figure (in control) to represent the dominance dimension. The participant can indicate any of the five figures comprising each scale, or any value in between two figures, resulting in a 9-point rating scale for each dimension. The Self-assessment Manikin has been proven to be a reliable instrument (Bradley & Lang, 1994).

*Physiological measures*

Ventilatory parameters were measured continuously with the LifeShirt System (VivoMetrics, Inc., Ventura, CA), implying inductive plethysmography. End-tidal $CO_2$ was monitored using a nasal $CO_2$-sampling cannula connected to the Oridion Microcap® Handheld Capnograph, with a sampling flow rate of 50 ml/min. The monitor uses Microstream non-dispersive infrared (NDIR) spectroscopy to continuously measure the partial pressure of $CO_2$ ($P\mathrm{et}CO_2$). We focused on $P\mathrm{et}CO_2$ because it is the most relevant indicator of hyperventilation. Electrodes for ECG measurement were attached to avoid demand effects (see Procedure).

*Procedure*

The patients were invited to participate in an experiment investigating physiological changes during imagery. When they agreed, they signed an informed consent. Next, they were asked to fill out the PSWQ, the

PANAS-state, and the Symptom Checklist, along with a 9-point scale to indicate their degree of fatigue at that moment (1 = not at all fatigued to 9 = very much fatigued).

Subsequently, the LifeShirt garment was put on and the ECG electrodes were attached. We used a cover story to avoid drawing the patient's attention to her breathing: the nose cannula for measuring $P\text{et}CO_2$ was described to measure the expired air temperature. The electrodes were explained to detect changes in posture and muscle tonus of the trunk.

The patient sat in a comfortable chair in a part of the room that was separated from the experimenter's place by a screen. The patient was asked to lean back in the seat, to keep both feet on the floor, and to place her hands on her legs. The experimenter checked whether she was comfortable, and it was stressed that the patient should keep the same position during the experiment.

The experimenter explained that four different imagery trials would follow, each consisting of the same consecutive phases. First, during a 1 min baseline period in which the lights were dimmed, the patient had to close her eyes and listen to relaxing music that was presented through headphones (Sarabande, Goldberg Suite, E. Grieg). During the following minute, the script was presented and the patient had to start imagery as soon as she heard the text. A 90 s silence period followed during which the patient had to keep on imagining the scene (after 60 s, a short low-level auditory signal, announced during the instructions, was given as a reminder to continue the imagery as vividly as possible). Finally, a 1 min recovery period followed in which the patient had to stop the imagery and listened to relaxing music (Gymnopédie no. 1, E. Satie), still with her eyes closed. At the end of the recovery period the lights were turned on.

The patients were asked to breathe through the nose as soon as the first imagery trial started. They were instructed to imagine the scenes as vividly as possible, not only creating a detailed visual picture of the scene, but also trying to experience the events as if they were a real, active participant in the scene. The patients were asked to specifically hold on to the feeling evoked by the last part of the script.

After the first practice trial, the experimenter discussed with the patient the extent to which she had succeeded in imagining the scene as an active participant. After this trial—as after each imagery trial—the patient rated the evoked images on the affective dimensions of valence, arousal, and dominance (Manikin). The vividness of the imagery, the ability to concentrate on the scripts, and the similarity of the evoked feelings to feelings in daily life were assessed by means of 9-point Likert scales. Then, the fatigue scale, the Symptom Checklist, and the PANAS state were administered referring to how the patient felt during the imagery period. It was explained that the presentation of the remaining three scripts would proceed in a similar fashion without any further intervention of the experimenter. Finally, we presented the ACFT and asked whether the patient had voluntarily controlled her breathing during one or more imagery trials. Afterwards, participants were fully debriefed.

### *Data analysis*

The data of the first practice trial (neutral script) were left out of the analyses. Raw waveform signals for physiological data were stored on a memory card and uploaded to a personal computer, calibrated, and reduced (parameter extraction, trend generation) by the VivoLogic software. This output was visually inspected before exporting the data to spreadsheets for further statistical processing. Only expirations with a clear alveolar plateau were used to determine $P\text{et}CO_2$ values.

Differences in fatigue scores between the different moments of measurement were investigated using repeated-measures ANOVA (four levels: baseline, relaxation script, acceptance script, and hostile resistance script). We used repeated-measures ANOVAs with script (three levels: R, ACC, and HR) as the within-subject variable for hyperventilation complaints, additional complaints, NA and PA scores, the subjective ratings of valence, arousal, dominance, imagery vividness, ability to concentrate on the script, and similarity with feelings in daily life.

For the physiological data, three phases were determined within each imagery trial: baseline (60 s); imagery phase (the last 30 s of script presentation and the 90 s of silence)[1]; and the recovery phase (60 s). To check for baseline differences, mean baseline $P\text{et}CO_2$ was analyzed in an ANOVA with script (R, ACC, and HR) as the within-subject variable. Next, we calculated change scores by subtracting the mean baseline $P\text{et}CO_2$ from the

[1]The first 30 s of the scripts contained a description of the situation (visit vs. store), whereas the last 30 s focused explicitly on the coping style (HR vs. ACC).

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mean $PetCO_2$ of the imagery phase. Subsequently, repeated-measures ANOVAs with script as the within-subject factor were performed on the change scores of the imagery phase. In addition, mean $PetCO_2$ of the R script, the ACC script, and the HR script was analyzed separately in repeated-measures ANOVAs including phase (three levels: baseline, imagery phase, and recovery phase) as the within-subject variable.

To check for the effects of specific script content (visit vs. store), script version was added as a between-subject variable to all analyses. For exploratory reasons, the tendency to worry (median split of PSWQ scores) and the attitude of (non)acceptance (median split of the ACFT scores) were added as between-subject variables to all analyses. Greenhouse–Geisser corrections were applied when appropriate and corrected degrees of freedom are reported. Follow-up comparisons between groups were made with either a priori tests or with Tukey HSD a posteriori tests. Pearson product–moment correlations were computed to further evaluate the relationships between the variables of interest. The $\alpha$ for all analyses was set at .05.

## Results

### *Manipulation checks*

There were no significant effects of the script version (visit vs. store), neither on the subjective data nor on $PetCO_2$. Consequently, the two versions of the script were considered equivalent and script version was omitted from all analyses. Because fatigue scores were not significantly different across measurement moments, the mental load of the experiment was no disturbing factor either. Analysis of the Manikin scales indicated a successful manipulation of the script content, in that patients felt less positive, more aroused, and less in control when placed in the HR script compared with the ACC and the R script. In addition, no significant differences between scripts were found for imagery vividness, ability to concentrate, and similarity to feelings in daily life (Table 1). None of the patients reported to have voluntarily controlled her breathing during the imagery trials.

Table 1
Mean and SD for valence, arousal, dominance, vividness, ability to concentrate, and similarity to feelings in daily life ($N = 30$)

| | R | Acc | HR |
|---|---|---|---|
| Valence | | | |
| M | 2.8[a] | 5.17[b] | 7.10[c] |
| SD | 1.92 | 2.2 | 1.47 |
| Arousal | | | |
| M | 7.53[a] | 6.5[b] | 4.77[c] |
| SD | 1.74 | 1.91 | 2.01 |
| Dominance | | | |
| M | 7.17[a] | 5.87[b] | 4.60[c] |
| SD | 2.09 | 2.69 | 2.06 |
| Vividness | | | |
| M | 6.47[a] | 6.63[a] | 6.57[a] |
| SD | 1.96 | 1.61 | 1.52 |
| Concentration | | | |
| M | 63.30[a] | 65.67[a] | 65.17[a] |
| SD | 23.96 | 22.08 | 23.02 |
| Similarity | | | |
| M | 6.03[a] | 5.97[a] | 6.3[a] |
| SD | 1.9 | 1.79 | 1.93 |

*Notes*: R = relaxation; Acc = acceptance; and HR = hostile resistance.
Low values represent imageries with positive valence, high arousal, low dominance, low vividness, low ability to concentrate on the script, and little similarity to feelings in daily life.
Means with the same superscripts are not significantly different ($p < .05$).

### Subjective data

#### Type of script

Imagining an action set of hostile resistance was associated with the highest level of hyperventilation complaints (Table 2). This level was significantly higher than when a state of acceptance or relaxation was imagined. Also, acceptance was associated with more hyperventilation complaints than relaxation. The additional complaints showed the same pattern, except that imagining acceptance did not produce more complaints than relaxation.

Comparable effects were obtained for NA. Imagining hostile resistance produced a level of NA that was significantly higher than imagining acceptance or relaxation. Acceptance also produced more NA than relaxation. PA was lower during hostile resistance than during acceptance or relaxation, whereas the latter did not differ (Table 2).

#### Tendency to worry

Overall, high worriers reported more hyperventilation complaints than low worriers (median split of PSWQ scores) [main effect: $F(1,27) = 7.62$, $p < .05$], but this difference was larger in the ACC and in the HR script compared with the R script, $F(1,27) = 7.02$ and 8.55, $p < .05$ and $< .01$, respectively [interaction effect: $F(1.77;47.72) = 4.07$, $p < .05$]. Within the group of high worriers, more hyperventilation complaints were reported during the HR script than during the R and the ACC script, $F(1,27) = 31.16$ and 9.72, respectively, $p$'s $< .01$; and more hyperventilation complaints were reported in the ACC than in the R script, $F(1,27) = 7.07$, $p < .05$. Within the group of low worriers, more hyperventilation complaints were reported in the HR compared with the R script, $F(1,27) = 4.47$, $p < .05$, but not compared with the ACC script (ns). There were no significant differences between the ACC script and the R script (ns) in this group (Fig. 1).

High worriers reported overall more additional complaints, $F(1,27) = 10.4$, $p < .01$, had higher NA scores, $F(1,28) = 10.53$, $p < .01$, and lower PA scores, $F(1,28) = 6.48$, $p < .05$, than low worriers.

#### Acceptance

An accepting attitude towards CFS (based on a median split of ACFT scores) had no effects on the reporting of complaints, nor on the PANAS scores during the experiment.

Table 2
Mean and SD for hyperventilation complaints, additional complaints, NA, and PA ($N = 30$)

| | R | Acc | HR | ($F$, df) |
|---|---|---|---|---|
| Hyperventilation complaints | | | | |
| M | $19.03^{a}$ | $21.07^{b}$ | $23.93^{c}$ | |
| SD | 6.01 | 6.39 | 9.48 | (13.39;1.73)** |
| Additional complaints | | | | |
| M | $36.28^{a}$ | $37.03^{a}$ | $39.00^{b}$ | |
| SD | 11.25 | 11.11 | 12.98 | (3.42;1.95)* |
| NA | | | | |
| M | $12.57^{a}$ | $17.27^{b}$ | $20.80^{c}$ | |
| SD | 4.99 | 7.04 | 8.09 | (28.81;1.92)** |
| PA | | | | |
| M | $20.17^{a}$ | $19.97^{a}$ | $17.23^{b}$ | |
| SD | 5.27 | 5.56 | 4.35 | (6.43;1.72)** |

*Notes*: R = relaxation; Acc = acceptance; and HR = hostile resistance.
Means with different superscripts are significantly different at $p < .05$.
*$p < .05$; **$p < .01$.

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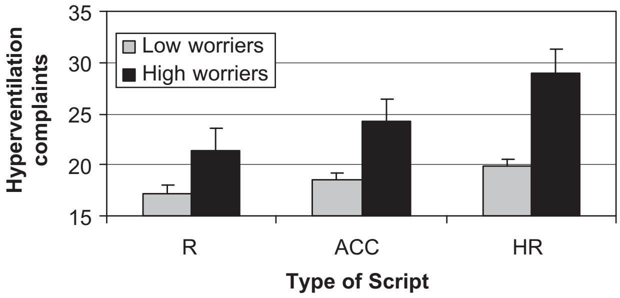


Fig. 1. Effect of worrying on the reporting of hyperventilation complaints.

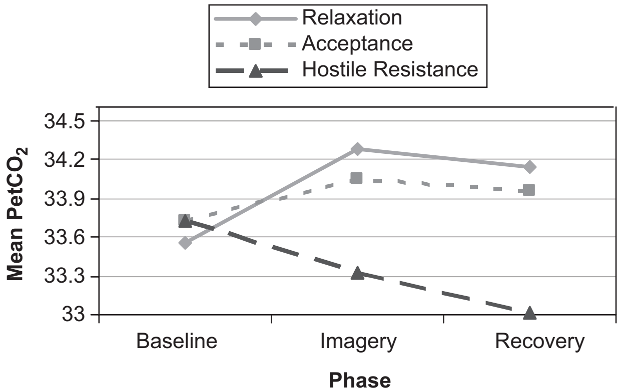


Fig. 2. Mean $P\text{etCO}_2$ in the different phases of each script.

*Physiological data*

Physiological data of four patients were lost because of equipment failure. The $P\text{etCO}_2$ values of the remaining 26 patients were analyzed.

*Baseline data*

Mean $P\text{etCO}_2$ at the start of the experiment was 33.47 mmHg ($\pm$3.75). No significant baseline differences were found in mean $P\text{etCO}_2$ among the three scripts.

*Type of script*

Type of script influenced the change scores in mean $P\text{etCO}_2$ of the imagery phase $F(1.54;38.40) = 9.8$, $p<.01$. During the HR script mean $P\text{etCO}_2$ decreased significantly stronger compared with baseline than during the R script, $F(1,25) = 12.66$, $p<.01$, and the ACC script, $F(1,25) = 14.04$, $p<.01$. There were no significant differences in change scores between the R script and the ACC script (ns).

The course of the mean $P\text{etCO}_2$ over the three consecutive phases of each script showed an interesting pattern. In the R script, mean $P\text{etCO}_2$ of patients increased from baseline to the imagery and the recovery phase [main effect: $F(1,68;42,01) = 6.94$, $p<.01$; Tukey test baseline to recovery: $p<.05$; imagery to recovery: ns]. In the ACC script, mean $P\text{etCO}_2$ remained stable (no significant differences). In contrast, in the HR script mean $P\text{etCO}_2$ was significantly lower during the recovery than during baseline [main effect: $F(1,26;31,52) = 3.55$; $p = .06$; Tukey: $p<.05$] (Fig. 2).

*Correlations*

Significant positive correlations between the amount of reported hyperventilation complaints and state NA were found in the ACC ($r = .38$, $p<.05$), and the HR script ($r = .74$, $p<.01$), but not in the R script ($r = .27$, ns). A significant negative correlation with state PA was observed in the HR script ($r = -.37$, $p = .05$). The correlation between the amount of reported additional complaints and state NA was only significant for the HR script ($r = .53$; $p < .01$). No significant correlations were found between the amount of reported hyperventilation or additional complaints and mean $P$et$CO_2$. For all scripts, there was a significant positive correlation between the score on the ACFT and mean $P$et$CO_2$. Finally, we found a significant negative correlation between similarity with feelings in daily life and mean $P$et$CO_2$ during the imagery phase of the HR script ($r = -.43$; $p < .05$).

## Discussion

We investigated the possible role of coping in the relationship between hyperventilation and CFS, using an imagery paradigm. Imagery of a hostile resistance action set caused a decrease in $P$et$CO_2$ as well as deficient recovery of $P$et$CO_2$. Furthermore, more symptoms were reported during hostile resistance compared with relaxation. In contrast, fewer symptoms were reported during an action set of acceptance and the tendency to accept chronic fatigue was positively related to mean $P$et$CO_2$. Although a positive impact of acceptance on subjective quality of life has been reported earlier (Viane et al., 2003; Van Damme et al., 2006), the present study is the first to show a significant positive relationship between acceptance and an objective physiological response parameter.

Overall, our patient group tended to have low resting values of $P$et$CO_2$, which makes them more vulnerable to developing complaints of hyperventilation. However, despite the script-related differences in both $P$et$CO_2$ and self-reported hyperventilation complaints, it is unlikely that hyperventilation was the actual cause of the complaints. First, the maximal difference in $P$et$CO_2$ was only about 1 mmHg. Although statistically significant, it is not clinically significant as it is not large enough to explain the differences in symptom reporting between scripts. Second, the changes between scripts were not confined to hyperventilation complaints, but also concerned additional complaints, which are not typically related to reduced $P$et$CO_2$. Finally, there was no significant negative correlation between the amount of reported hyperventilation complaints and mean $P$et$CO_2$ during imagery.

In addition, script-related differences in complaints mirrored differences in state NA perfectly, suggesting that our findings are an exemplar of the general finding that persons with high negative affectivity—a tendency to experience negative emotional states—report more medically unexplained symptoms (Watson & Pennebaker, 1989). The link between NA and elevated symptom reports most likely reflects the effect of schema-driven processing of interoceptive information in which affective rather than somatic cues are used to determine the subjective somatic state. It has been shown that affective cues, previously associated with symptom episodes, may automatically trigger elevated symptom reports upon subsequent confrontations with these cues as a result of learning (Van den Bergh, Stegen, & Van de Woestijne, 1997, 1998). This leads to reduced interoceptive accuracy (Bogaerts et al., 2005). Furthermore, the relation between negative affect and subjective symptoms may be related to partly shared or overlapping brain areas, subserving emotional and visceral interoception (Critchley, Mathias, & Dolan, 2001).

Our results suggest that occasional hyperventilation may occur in CFS patients, especially in conditions of hostile resistance. Subsequent engagement in this type of action set may provide affective cues triggering a subjective experience of hyperventilation complaints as a learned response in the absence of hypocapnia. Given the similarity between hyperventilation and CFS complaints, these elevated symptom episodes may be experienced by the patient as additional evidence for the poor prognosis and stimulate related illness behavior, such as prolonged inactivity leading to physical deconditioning (Sharpe, Hawton, Seagroatt, & Pasvol, 1992).

Another interesting finding was that, for the relaxation and the acceptance script, $P$et$CO_2$ tended to return to baseline level after imagery, whereas for the hostile resistance script, a further decrease in $P$et$CO_2$ occurred. This deficient recovery of $P$et$CO_2$ after imagery of hostile resistance in CFS patients is quite remarkable, because previous imagery studies in our group, using relaxation and fear-inducing scripts, found normal recovery of $P$et$CO_2$ to baseline level in normals, even after a significant decrease in $P$et$CO_2$ during imagery of the fear script (Van Diest et al., 2001). Delayed recovery of $PCO_2$ has previously been found after voluntary hyperventilation induction in patients with chronic hyperventilation syndrome and panic disorder patients (Han et al., 1997; Wilhelm, Gerlach, & Roth, 2001). Their slow recovery was not specific to the respiratory system, but also applied to autonomic and self-report measures. Our findings add to this that the deficient recovery of $P$et$CO_2$ in CFS patients occurs when breathing spontaneously, without a mouthpiece and without preceding forced changes in the breathing pattern, and it only occurred in specific conditions, namely when imagery induced major increases in negative affect.

It is currently not clear how to account for this observation in CFS patients. It either points to breathing regulation problems in CFS, comparable to those found in panic and hyperventilation patients, or it points to the role of cognitive processes prolonging the effects of imagining the hostile resistance script. For example, CFS patients have been shown to have a strong focus on internal states (Wood, Bentall, Gopfert, & Edwards, 1991). Previous research has also shown an association between NA and a decreased ability to shift to a new focus (Compton, 2000). The deficient recovery in the hostile resistance script might suggest that CFS patients have more difficulty disengaging attention from minor bodily sensations, resulting in a less adaptive response to stress (Hoehn-Saric & McLeod, 2000).

The tendency to worry had a negative moderating influence on symptom reporting. Our findings endorse research with chronic pain patients providing evidence that worrying has a negative impact on complaints and experienced pain (Aldrich, Eccleston, & Crombez, 2000).

This study has some limitations. First, our sample was confined to women only. Despite CFS being more prevalent in women than in men (Jason et al., 1999), it would be interesting to know whether our findings generalize to men. Gender-related differences exist in symptom reporting (Gijsbers van Wijk, Huisman, & Kolk, 1999), symptom perception processes (Roberts & Pennebaker, 1995), and in stress physiology (Taylor et al., 2000). Secondly, our patient group was treatment-seeking and had not yet received behavioral interventions. Results from these patients may not generalize to non-treatment-seekers, or patients at post-treatment. Thirdly, in our experiment no independent control group was used. However, one of the problems in research comparing acceptance as a general attitude between different groups is that it may covary with, e.g., self-efficacy or a wide range of other patient characteristics that are hard to control. The strength of the present study design is that scripts were used that were emotionally relevant to CFS patients to induce different attitudes within one and the same person. Finally, both action sets of ‘‘acceptance’’ and ‘‘hostile resistance’’ may be correlated with a whole range of other psychological processes, such as positive, or negative/hostile thinking, respectively. Defining more precisely which psychological processes during both attitudinal sets are exactly responsible for the observed effects is an important focus for future research.

In summary, CFS patients adopting an action set of hostile resistance towards their illness report more negative affect, more subjective complaints, and tend to hyperventilate, which may last and aggravate beyond the duration of actively adopting this action set. Conversely, adopting an action set of acceptance is associated with less negative affect, less subjective complaints, and no hyperventilation. Our results suggest that the promotion of acceptance as a coping strategy may have good additive value to the existing revalidation program, which currently consists of traditional cognitive behavioral therapy and graded exercises.

## Acknowledgment

The first author is supported by the Research Foundation—Flanders (FWO-Vlaanderen).

## Appendix A. Supplementary materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.brat.2007.07.003.

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Please cite this article as: Bogaerts, K., et al. Hyperventilation in patients with chronic fatigue syndrome: The role of coping strategies. *Behaviour Research and Therapy* (2007), doi:10.1016/j.brat.2007.07.003