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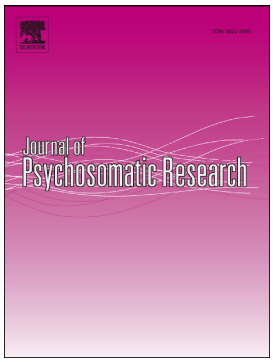

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Retrospective memory for symptoms in patients with medically unexplained symptoms

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Abstract

Objective: Clinical assessment and diagnostic processes heavily rely on memory-based symptom reports. The current study investigated memory for symptoms and the peak-end effect for dyspnea in patients with medically unexplained symptoms and healthy participants.

Methods: Female patients with medically unexplained dyspnea (MUD) (n = 22) and matched healthy controls (n = 22) participated in two dyspnea induction trials (short, long). Dyspnea ratings were collected: (1) continuously during symptom induction (concurrent with respiratory measures), (2) immediately after the experiment, and (3) after 2 weeks. Symptoms, negative affect, and anxiety were assessed at baseline and after every trial. The mediating role of state anxiety in symptom reporting was assessed. The peak-end effect was tested with forced-choice questions measuring relative preference for the trials.

Results: Compared to controls, dyspnea induction resulted in higher levels of symptoms, anxiety, concurrent dyspnea ratings, and minute ventilation in the patient group. In both groups, immediate retrospective ratings were higher than averaged concurrent ratings. No further increase in dyspnea ratings was observed at 2-week recall. Retrospective dyspnea ratings were mediated by both state anxiety and concurrent dyspnea ratings. Patients did not show a peak-end effect, whereas controls did.

Conclusion: The findings show that patients' experience of a dyspneic episode is subject to immediate memory bias, but does not change over a longer time period. The results also highlight the importance of affective state during symptom experience for both symptom perception and memory.

Keywords: Dyspnea, peak-end effect, medically unexplained symptoms, memory, anxiety, self-report

Introduction

In health care, patients are repeatedly asked to report about their symptoms. These reports can pertain to concurrent and retrospective symptom experiences. Whereas factors biasing symptom perception have been thoroughly documented for patients with medically unexplained symptoms (MUS) [1–3], little attention has been given hitherto to symptom memory, despite the fact that clinical assessments and questionnaire studies largely rely on memory-based responses.

Studies involving both patient and healthy populations have consistently shown that symptom recall is typically overestimated [see 4,5 for reviews]. However, only a few studies explored memory processes among patients with MUS [6,7]. In one study, it was shown that the peak-end effect, while quite robust in general [8–12], was absent in patients with medically unexplained dyspnea (MUD) after induced dyspneic episodes [6]. The peak-end effect is a cognitive heuristic implying that retrospective evaluation of an aversive episode is determined by the most distressing (peak) and the final (end) moments of the experience, and less so by its duration [11]. In another study [7], patients with MUD recalled fewer specific health-related autobiographical memories than healthy controls. These findings suggest that somatic episodes are processed and represented in memory with less sensory-perceptual detail in patients with MUS compared to controls. Interestingly, there is also consistent evidence that patients with MUS are not only more anxious [13–15], but also show exaggerated affective responses to somatic events [16,17]. The combined effect of less detailed processing of sensory-perceptual aspects of a somatic episode and exaggerated affective responses to it may make persons with MUS particularly vulnerable to retrospective memory distortions. This fits with findings in non-clinical groups showing that retrospective ratings of daily symptoms

and experimentally induced dyspnea increase over time in high compared to low habitual symptom reporters [12,18] and that this increase is mediated by affective responses to the somatic event [12,19].

The distinction between sensory-perceptual and affective-motivational components in symptom reporting is in accordance with neurobiological [20], behavioral [21], and psychometric research [22–24] and may be highly relevant to understand MUS and biases in retrospective symptom memory. According to a recent predictive coding model accounting for MUS, exaggerated affective responses and reduced sensory-perceptual processing result in less precise prediction errors related to somatic input, making symptom experiences more vulnerable to become dominated by strong priors (predictions) and, as such, become dissociated from physiological dysfunction [3]. In line with this, we assume that the affective-motivational component during a somatic episode will have greater influence on symptom ratings in patients with MUS. Moreover, its impact would also become more dominant over time [19], due to time-dependent effects of emotion on symptom memory [25–27] and memory processes in general [28,29].

In the present study, we examined how symptom ratings of an experimentally induced dyspneic episode change over time among patients with MUD complaints, also known as behavioral dyspnea [6,30]. Patients with MUD are characterized by a number of symptoms in different bodily systems, such as urge to breathe, chest tightness, and fatigue that do not originate from an underlying cardiovascular or respiratory disorder. The symptoms are experienced as distressing and disruptive and are associated with excessive worrying, anxiety, and frequent medical consultations [16,17,30]. We also wanted to replicate the absence of a peak-end effect in MUD patients. Therefore, dyspnea was induced in two rebreathing trials

[31]. A short trial ended at the most intense level of dyspnea, whereas a long trial additionally included a partial recovery period. Relative preference for the trials (if they were to be repeated) was assessed as a test of the peak-end effect [6,11], which typically shows up as a preference for the long trial relative to the short, despite more overall distress in the long trial. Participants rated experienced dyspnea concurrently during the induction trials, immediately after the experiment, and after two weeks. Based on abovementioned arguments, our predictions were: (1) Patients would rate concurrent dyspnea as more intense than healthy controls; (2) Immediate retrospective dyspnea ratings would be higher than concurrent ratings, with greater overreporting in patients; (3) Retrospective ratings would increase over time only in patients; (4) This overreporting would be mediated by the affective responses to the dyspnea trials; (5) The peak-end effect would be observed in the control but not in the patient group [replicating 6].

Methods

Participants

The study was part of a larger two-part questionnaire and experimental study investigating memory in patients with medically unexplained dyspnea (MUD). The data from the questionnaire study are reported elsewhere [7]. The Medical Ethics Committee of the University Hospital of the University of Leuven approved the protocol. A €15 reimbursement was provided to the participants.

Participants in the patient group (n = 30, all women) were recruited from the outpatient pulmonology clinic of the Leuven University Hospital (Gasthuisberg). Patients were classified as having MUD after a systematic medical work-up procedure which excluded organic reasons for multiple somatic symptoms such as breathing distress, dyspnea, numbness, and fatigue, and after a systematic interview

(the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Axis I Disorders [32]) by a qualified psychologist which excluded psychiatric causes for experienced dyspnea other than somatization disorder. Exclusion criteria were: a self-reported history of pulmonary, cardiovascular, gastrointestinal, or neuromuscular disease; medical conditions that likely affect respiratory capacity, such as acute illnesses, fever, or flu; mental disorder other than somatoform disorder (self-reported via a general item); pregnancy or breastfeeding.

Two patients reported use of selective serotonin reuptake inhibitors (escitalopram, sertraline). Healthy controls (n = 24, all women) were recruited via local advertisements and matched for age, body mass index, and education level. To be included in the study, they also had to score < 75 on the Checklist for Symptoms in Daily Life [24,33]. Two controls and eight patients were excluded from the analyses because of technical difficulties (e.g., unstable filter) or problems with completing the experiment as instructed (e.g., stopping the trial, not returning the follow-up questionnaires). Therefore, reported results are based on data from 22 patients and 22 controls. The groups did not differ with regard to demographic characteristics (Table 1).

Measures

Self-reported measures

Negative affectivity. Trait and state negative affectivity (NA) were measured with the Dutch version of the Positive and Negative Affect Schedule [34,35]. Using a 5-point Likert scale ranging from *not at all* to *very much*, participants rated to what extent they experience 10 positive and 10 negative emotions in general (trait) or now (state). Cronbach's alphas for both trait and state versions ranged from .83 to .92.

Depression. Depression was measured with the Dutch version of Beck Depression Inventory-II (BDI-II) [36], a 21-item questionnaire assessing cognitive, affective, and physical symptoms of depression in the past 2 weeks. Cronbach's alpha was .93.

Habitual symptom reporting. Habitual symptom reporting was measured by the adapted version of the Checklist for Symptoms in Daily Life (CSD) [24,33]. Participants rate how often they experienced 39 symptoms in the past year on a 5-point Likert scale (*never*, *seldom*, *sometimes*, *often*, *very often*). Cronbach's alpha was .96.

State symptom and affect ratings. As in a previous study using a rebreathing paradigm [37], a state symptom checklist assessed symptoms experienced during the trial. Participants rated 46 symptoms on a 5-point rating scale: *not at all* to *very much*. Cronbach's alphas ranged from .93 to .96. State anxiety was evaluated with a single item numerical rating scale (1 = *not at all anxious*, 9 = *very anxious*).

Concurrent dyspnea ratings. During each trial, concurrent dyspnea was rated every 10s on a vertical 0-100 computerized scale marked with descriptive terms based on a modified Borg scale [38]: *none* (0), *very slight* (10), *slight* (20), *moderate* (30), *fairly severe* (40), *severe* (50), *very severe* (60), *very severe* (70), *very severe* (80), *very, very severe* (90), *intolerable* (100).

Retrospective dyspnea ratings. Retrospective ratings of average dyspnea experienced during each trial were collected at two moments: at the end of the experimental session (immediate rating) and after two weeks (follow-up rating). Participants indicated the average dyspnea level experienced during the trial on a visual analog scale (10cm) ranging from 0 (*no dyspnea*) to 100 (*maximum dyspnea*).

Forced-choice questions. As in previous studies [6,11], the peak-end effect was assessed after the two trials with forced-choice questions (see Table 2 for question descriptions). The peak-end effect was indicated by the preference for the experience in which the peak intensity was followed by a period of lower intensity (long trial) over the experience that ended at the same peak level (short trial).

Apparatuses and Physiological Recordings

Dyspnea was induced with the rebreathing paradigm [6,12,19,31]. During the trials, participants wore a nose clip and breathed through a mouthpiece, connected to the rebreathing bag with a wide vinyl tube and a Y-valve ending on a pneumotachograph (Fleisch no. 2, Lausanne, Switzerland) measuring airflow. The valve enabled to change between room air and the rebreathing bag, which was filled with 5-liter gas mixture of 5% CO_2 and 95% O_2. The exhaled air was sampled close to the mouthpiece to determine the fractional end-tidal concentration of CO_2 ($FetCO_2$), measured by an infrared CO_2 monitor (POET RC, Criticare Systems Inc., Waukesha, WI). The data from the pneumotachograph and the CO_2 monitor were sampled at 20Hz, stored on a computer, and analyzed offline to define minute ventilation (MV) in L/min and $FetCO_2$ in %.

Procedure

Prior to the laboratory session (Figure 1), participants completed an at-home assessment including the trait questionnaires (CSD, PANAS, BDI-II). Participants were required to refrain from coffee, tea, or alcohol after midnight before participating and not to smoke for at least 2 hours before the experiment.

Upon arrival, participants were informed that they would inhale three different air mixtures. After signing informed consent, participants completed the state questionnaires (PANAS, symptom checklist, anxiety). Afterwards, participants were

familiarized with the procedure and equipment during a practice trial with room air, followed by the two rebreathing trials presented in a counterbalanced order. The short trial comprised a baseline phase (60 s of room-air breathing) and a rebreathing phase (150 s), after which the trial was terminated. The long trial consisted of the same baseline and rebreathing phases, followed by an additional recovery phase (150 s), during which participants were breathing room air while continuing to provide concurrent dyspnea ratings. State questionnaires were administered after each trial. A 15-min intertrial pause allowed recovery from the trial.

After completion of both trials, participants were informed that additional information was required prior to the final trial. They were presented with forced-choice preference questions, after which they were informed that the third trial was unnecessary. Finally, immediate retrospective dyspnea ratings were collected.

Two weeks following the experiment, participants completed a follow-up assessment at home consisting of follow-up retrospective dyspnea ratings of both trials and mailed it back.

Data analyses

The group differences in demographic variables and trait measures were assessed using χ^2 and *t*-tests. Group differences in state symptoms, NA, and anxiety ratings were examined with mixed analyses of variance (ANOVA) with Trial (baseline/short trial/long trial) as within-subject factor and Group (patients/controls) and Trial Order as between-subject factors.

Concurrent dyspnea ratings and respiratory responses ($FetCO_2$, MV) during each trial were averaged per 30 s for each participant and examined in separate mixed ANOVAs with Time Segment as a within-subject factor and Group and Trial Order as between-subject factors. The dyspnea ratings over a 2-week period were

analyzed with mixed ANOVA with Dyspnea Trial (short/long) and Time (averaged concurrent/immediate/follow-up) as within-subject factors and Group and Trial Order as between-subject factors. For this analysis, concurrent dyspnea ratings were averaged per trial. Group differences in change in dyspnea ratings over time were examined with planned contrasts that compared concurrent versus immediate ratings and immediate versus follow-up ratings.

To examine whether the group differences in retrospective ratings were associated with state anxiety during the trials, multiple-mediator models were applied to follow-up dyspnea ratings of both trials. Both state anxiety and averaged concurrent dyspnea ratings were simultaneously included as mediators and tested in a single parallel multiple-mediator model using the bootstrapping procedure [39]. This method estimates both the indirect effects of the group on follow-up ratings through each of the mediators and the direct effects of the group. The 95% confidence intervals of the effects were derived with 5000 bootstrap resamples. Direct and indirect effects are reported in unstandardized form [40].

To assess the peak-end effect within each group and the differences between the groups with regard to forced-choice questions, Pearson χ^2 tests were applied.

Greenhouse–Geisser corrections were applied when the sphericity assumption was violated. Data were analyzed with IBM SPSS Statistics 24 and the PROCESS Macro for SPSS [40].

Results

Although no differences between the groups were observed for demographic characteristics, patients reported significantly higher levels of trait NA, BDI-II, and habitual symptom compared with controls (Table 1). Patients also reported more state symptoms and NA than controls (Table 3). The patient group not only reported

higher state anxiety in general, but their anxiety also increased more after the rebreathing trials compared to controls (Table 3).

Concurrent dyspnea ratings and respiratory responses

Patients reported significantly more dyspnea than controls during both the short, $F(1, 40) = 13.60$, $p = .001$, $\eta_p^2 = .25$, and the long trial, $F(1, 40) = 15.05$, $p < .001$, $\eta_p^2 = .27$ (Figure 2, upper panel). This difference became stronger over time in both trials, Group × Time Segment interaction in the short, $F(1.70, 68.17) = 13.73$, $p < .001$, $\eta_p^2 = .26$, and in the long trial, $F(2.68, 107.28) = 4.85$, $p = .005$, $\eta_p^2 = .11$.

Furthermore, patients had a higher mean MV than controls in both the short, $F(1, 39) = 4.32$, $p = .044$, $\eta_p^2 = .10$, and the long trial $F(1, 40) = 5.64$, $p = .022$, $\eta_p^2 = .12$ (Figure 2, middle panel). This difference changed over time both in the short and long trial: Group × Time Segment interaction, $F(1.31, 51.07) = 4.97$, $p = .022$, $\eta_p^2 = .11$, and $F(2.05, 82.04) = 3.12$, $p = .048$, $\eta_p^2 = .07$, respectively. No group-related differences were found for $FetCO_2$ (Figure 2, bottom panel).

In additional analyses, we included state anxiety as a covariate in the mixed ANOVAs of concurrent ratings and respiratory responses. Doing this, the previously observed group effects became non-significant.

Retrospective dyspnea ratings

Dyspnea ratings changed over time, $F(2, 80) = 55.05$, $p < .001$, $\eta_p^2 = .58$ (Figure 3). Planned contrasts indicated that immediate retrospective dyspnea ratings were higher than the averaged concurrent ones, $F(1, 40) = 69.40$, $p < .001$, $\eta_p^2 = .63$. However, the ratings did not further increase over the course of 2 weeks, planned contrast: $F(1, 40) = 0.62$, $p = .44$, $\eta_p^2 = .02$. Although patients reported more dyspnea than controls on all occasions, $F(1, 40) = 12.82$, $p = .001$, $\eta_p^2 = .24$, the expected

increase in dyspnea ratings over time among patients was not observed, Group × Time: $F(2, 80) = 1.50$, $p = .23$, $\eta_p^2 = .04$.

The mediating role of state anxiety

Multiple-mediator models for both trials are presented in Figure 4. In the short trial, specific indirect effects for both state anxiety, $a_1b_1 = 10.41$ (95% CI [1.66, 22.47]) and concurrent dyspnea ratings, $a_2b_2 = 11.80$ (95% CI [4.48, 22.74]) on follow-up ratings were significant. The effects did not differ in size, with the point estimate for the contrast between the two indirect effects, -1.38 (95% CI [-16.61, 13.06]), not significantly different from zero.

A similar pattern was found for the long trial, with significant specific indirect effects on follow-up ratings for both state anxiety, $a_1b_1 = 13.81$ (95% CI [4.04, 29.70]) and concurrent dyspnea ratings, $a_2b_2 = 8.35$ (95% CI [.76, 21.25]). The point estimate for the contrast between the two indirect effects, 5.47 (95% CI [-13.29, 24.64]), indicated that the effects did not differ in size.[1]

The peak-end effect

The frequencies on each of the forced-choice questions are shown in Table 2. Significant group differences were found only for the question concerning the greatest discomfort, with the peak-end effect only emerging in the control group (the short trial chosen as the one causing greatest discomfort). Within-group analyses also showed that the control group chose the short trial as causing greatest distress

[1] As the group differences in psychological characteristics could also affect the association between group and retrospective ratings, additional analyses including trait NA and depression as mediators were performed in abovementioned multiple-mediator models. Indirect effects through either trait NA or depression were nonsignificant. Adding these moderators did not affect the reported results.

at the peak and greatest dyspnea at the peak (marginal significance). The peak-end effect was absent in the patient group.

Discussion

The present study investigated memory for somatic symptoms among patients with MUD complaints. To this end, concurrent and retrospective ratings of induced dyspnea in patients with MUD and healthy controls were compared. Additionally, we measured physiological and affective responses to the stimuli. In accordance with previous findings, this study showed that patients with MUD reported more negative affective responses to the dyspnea episode as well as higher concurrent and retrospective dyspnea ratings than healthy controls. However, the difference between ratings collected immediately after the episode and averaged concurrent ratings was similar in both groups and retrospective reports did not increase over time in either of the groups. The absence of a peak-end effect was confirmed among patients with MUD.

Patients reported higher levels of concurrently experienced dyspnea than controls and this difference in self-report coincided with higher MV in the patient group, replicating previous findings [16,41]. Also consistent with earlier studies [16,17], patients felt more anxious not only at baseline, but also after the induction trials. Interestingly, when state anxiety experienced during the trials was taken into account in post-hoc analyses, the group-related differences in both self-report and physiological measures were no longer significant. This suggests that patients, being more prone to experience negative affective states, exhibited a more anxious response to the induction, which in turn led to an increase in MV and elevated dyspnea ratings. However, the increased MV did not impact the level of $FetCO_2$, which is a critical respiratory parameter for dyspnea. This pattern of data is in

accordance with a predictive coding perspective on MUS: these patients experience more anxiety during a somatic episode, resulting in less precise somatic prediction errors which makes them more vulnerable than controls to the influence of strong prior expectations [3,16].

Considering the retrospective ratings, an immediate retrospective overestimation of experienced dyspnea was present in both groups, confirming a discrepancy between the memory-based and concurrent ratings [12,42,43]. We hypothesized that patients' increased negative affective and diminished sensory-perceptual processing of bodily stimuli [3] would lead to better encoding of aversive quality of the episode and, consequently, more biased retrospective ratings. Although patients reported in general more dyspnea than controls, in contrast to our expectations and previous findings [12], the degree of overestimation did not differ between the groups. One possible explanation of this difference is that the stronger affective responses in patients resulted in a faster and deeper breathing pattern as indicated by the elevated MV. This may have produced more salient sensory-perceptual information to encode during the dyspneic episode, hence attenuating the relative impact of the affective-motivational response [21]. The degree in which affective responses influence physiological reactions and, subsequently, sensory input, may be larger in this patient group than in non-clinical high HSR. Indeed, in a previous study [12] with the same rebreathing paradigm, non-clinical HSR individuals showed an increase in dyspnea overreporting over time, but they did not differ in MV during the dyspnea induction.

This interpretation may also shed light on another unanticipated finding, namely that retrospective dyspnea ratings did not increase over the course of two weeks, neither in the patient (as was found in non-clinical HSR individuals, 12) nor in

the control group. This prediction was based on earlier findings showing that the effects of a negative affective state on symptom memory increase over time [19,26,27]. However, as relatively more sensory-perceptual input (elevated MV) was produced by patients than by controls during the encoding of experience, the hypothesized relative dominance of affective compared to sensory information in symptom memory of patients may have been reduced. Our mediation analyses are consistent with this interpretation: both the concurrent dyspnea ratings and state anxiety were equally strong and significant mediators of the association between the experimental group and retrospective dyspnea ratings. Those mediators were also highly intercorrelated, making it difficult to disentangle their relative effects (short trial: $r(42) = .71$, $p < .001$; long trial: $r(42) = .75$, $p < .001$).

Finally, we replicated the absence of the peak-end effect in patients whereas it appeared in the healthy controls [6]. This confirms the differences between patients and healthy persons in the way they encode and retrospectively evaluate dyspneic episodes. However, our results are less consistent across the entire set of preference questions compared to what was found in a previous study [6]. One reason for these weaker effects may be related to the interpretation advanced above, namely that the elevated anxiety of patients during the dyspnea induction also produced more intense physiological responses, resulting in a better encoding of detailed sensory-perceptual input. A peak-end effect may fail to occur when the experience is dominated by a non-differentiated distress response to dyspnea, and may gradually appear when more sensory-perceptual details become available, weakening to some extent the difference between patients and controls.

A key strength of the present study was an inclusion of concurrent and retrospective symptom ratings over a substantial follow-up period, together with an

assessment of physiological responses to a standardized and validated dyspnea induction paradigm. Exploring the issue of memory for symptoms in both clinical and control group is an important addition to the previous studies, which very often focused only on the patient groups [43,44].

The current study also has some limitations. First, our participant sample was limited to women. Gender-related differences were consistently observed in symptom reporting [45,46], including responses to a dyspneic episode [47]. Given the increased prevalence of medically unexplained symptoms in women [48,49], we relied on a female sample to avoid an uneven gender distribution. Second, due to the small sample size the study may be somewhat underpowered to detect the difference between the retrospective dyspnea ratings. Therefore, the findings should be replicated with a larger and more diverse sample and considered preliminary. Third, retrospective ratings were collected only at the end of the experiment and not immediately after the trial. Although biased symptom reporting can occur at this early stage, the difference between immediate and end-of-experiment ratings was previously reported to be minor [12]. Also, this study focused on patients with medically unexplained symptoms, which in the DSM-IV were classified under somatoform disorder. However, the DSM-5 [50] omitted the distinction between medically explained and unexplained symptoms in the new diagnosis of somatic symptom disorder. It remains to be explored whether the memory effects differ between patients with MUS and patients with symptoms linked to a biomedical dysfunction. Finally, future studies should examine whether observed effects with dyspnea generalize to other somatic symptoms such as pain or fatigue.

The current findings add to a growing body of literature on cognitive and affective processes characterizing patients with MUS. Our findings highlight the

important role of affective state in both concurrent and retrospective reporting of dyspnea suggesting that interventions modulating emotional appraisal to symptom episodes might reduce symptom recall bias [19,51]. We also confirm the absence of a peak-end effect in symptom evaluations in patients with MUS. This suggests that the way these patients encode and recall a somatic event may be a robust and critical marker of their condition. However, further investigations are needed to fully understand the underlying mechanisms.

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References

[1] W. Rief, E. Broadbent, Explaining medically unexplained symptoms-models and mechanisms, Clin. Psychol. Rev. 27 (2007) 821–841. doi:10.1016/j.cpr.2007.07.005.

[2] R.J. Brown, Psychological mechanisms of medically unexplained symptoms: An integrative conceptual model, Psychol. Bull. 130 (2004) 793–812. doi:10.1037/0033-2909.130.5.793.

[3] O. Van den Bergh, M. Witthöft, S. Petersen, R.J. Brown, Symptoms and the body: Taking the inferential leap, Neurosci. Biobehav. Rev. 74 (2017) 185–203. doi:10.1016/j.neubiorev.2017.01.015.

[4] O. Van den Bergh, M. Walentynowicz, Accuracy and bias in retrospective symptom reporting, Curr. Opin. Psychiatry. 29 (2016) 302–308. doi:10.1097/YCO.0000000000000267.

[5] D.E. Stull, N.K. Leidy, B. Parasuraman, O. Chassany, Optimal recall periods

for patient-reported outcomes: Challenges and potential solutions, Curr. Med. Res. Opin. 25 (2009) 929–942. doi:10.1185/03007990902774765.

[6] K. Bogaerts, L. Wan, I. Van Diest, L. Stans, M. Decramer, O. Van den Bergh, Peak-end memory bias in laboratory-induced dyspnea, Psychosom. Med. 74 (2012) 974–981. doi:10.1097/PSY.0b013e318273099c.

[7] M. Walentynowicz, F. Raes, I. Van Diest, O. Van den Bergh, The specificity of health-related autobiographical memories in patients with somatic symptom disorder, Psychosom. Med. 79 (2017) 43–49. doi:10.1097/PSY.0000000000000357.

[8] E. Chajut, A. Caspi, R. Chen, M. Hod, D. Ariely, In pain thou shalt bring forth children: The peak-and-end rule in recall of labor pain, Psychol. Sci. 25 (2014) 2266–2271. doi:10.1177/0956797614551004.

[9] D.A. Redelmeier, D. Kahneman, Patients' memories of painful medical treatments: Real-time and retrospective evaluations of two minimally invasive procedures, Pain. 66 (1996) 3–8. doi:10.1016/0304-3959(96)02994-6.

[10] D.A. Redelmeier, J. Katz, D. Kahneman, Memories of colonoscopy: A randomized trial, Pain. 104 (2003) 187–194. doi:10.1016/S0304-3959(03)00003-4.

[11] D. Kahneman, B.L. Fredrickson, C.A. Schreiber, D.A. Redelmeier, When more pain is preferred to less: Adding a better end, Psychol. Sci. 4 (1993) 401–405. doi:10.1111/j.1467-9280.1993.tb00589.x.

[12] M. Walentynowicz, K. Bogaerts, I. Van Diest, F. Raes, O. Van den Bergh, Was it so bad? The role of retrospective memory in symptom reporting, Heal. Psychol. 34 (2015) 1166–1174. doi:10.1037/hea0000222.

[13] P. Henningsen, T. Zimmermann, H. Sattel, Medically unexplained physical

symptoms, anxiety, and depression, Psychosom. Med. 65 (2003) 528–533. doi:10.1097/01.PSY.0000075977.90337.E7.

[14] J. van Eck van der Sluijs, M. ten Have, C. Rijnders, H. van Marwijk, R. de Graaf, C. van der Feltz-Cornelis, Medically unexplained and explained physical symptoms in the general population: Association with prevalent and incident mental disorders, PLoS One. 10 (2015) 1–14. doi:10.1371/journal.pone.0123274.

[15] E. Constantinou, K. Bogaerts, L. Van Oudenhove, J. Tack, I. Van Diest, O. Van den Bergh, Healing words: Using affect labeling to reduce the effects of unpleasant cues on symptom reporting in IBS patients, Int. J. Behav. Med. 22 (2015) 512–520. doi:10.1007/s12529-014-9449-8.

[16] L. Wan, L. Stans, K. Bogaerts, M. Decramer, O. Van den Bergh, Sensitization in medically unexplained dyspnea: Differential effects on intensity and unpleasantness., Chest. 141 (2012) 989–995. doi:10.1378/chest.11-1423.

[17] J. Han, Y. Zhu, S. Li, D. Luo, H. Zheng, I. Van Diest, S. De Peuter, K.P. Van de Woestijne, O. Van den Bergh, Medically unexplained dyspnea: Psychophysiological characteristics and role of breathing therapy., Chin. Med. J. (Engl). 117 (2004) 6–13.

[18] J.H. Houtveen, N.Y.L. Oei, Recall bias in reporting medically unexplained symptoms comes from semantic memory, J. Psychosom. Res. 62 (2007) 277–282. doi:10.1016/j.jpsychores.2006.11.006.

[19] M. Walentynowicz, I. Van Diest, F. Raes, O. Van den Bergh, Ways of encoding somatic information and their effects on retrospective symptom reporting, Br. J. Health Psychol. 22 (2017) 362–378. doi:10.1111/bjhp.12234.

[20] A.D. Craig, A new view of pain as a homeostatic emotion, Trends Neurosci. 26

(2003) 303–307. doi:10.1016/S0166-2236(03)00123-1.

[21] H. Leventhal, D. Brown, S. Shacham, G. Engquist, Effects of preparatory information about sensations, threat of pain, and attention on cold pressor distress., J. Pers. Soc. Psychol. 37 (1979) 688–714. doi:10.1037//0022-3514.37.5.688.

[22] M. Witthöft, W. Hiller, N. Loch, F. Jasper, The latent structure of medically unexplained symptoms and its relation to functional somatic syndromes, Int. J. Behav. Med. 20 (2013) 172–183. doi:10.1007/s12529-012-9237-2.

[23] M. Witthöft, S. Fischer, F. Jasper, F. Rist, U.M. Nater, Clarifying the latent structure and correlates of somatic symptom distress: A bifactor model approach., Psychol. Assess. 28 (2016) 109–115. doi:10.1037/pas0000150.

[24] M. Walentynowicz, O. Van den Bergh, M. Witthöft, F. Raes, I. Van Diest, Sensory and affective components of symptom perception: A psychometric approach, J. Exp. Psychopathol. (2017). doi:10.5127/jep.059716.

[25] G. Kent, Memory of dental pain, Pain. 21 (1985) 187–194. doi:10.1016/0304-3959(85)90288-X.

[26] J.J. Gedney, H. Logan, Memory for stress-associated acute pain, J. Pain. 5 (2004) 83–91. doi:10.1016/j.jpain.2003.11.005.

[27] J.J. Gedney, H. Logan, R.S. Baron, Predictors of short-term and long-term memory of sensory and affective dimensions of pain., J. Pain. 4 (2003) 47–55. doi:10.1054/jpai.2003.3.

[28] T. Sharot, E.A. Phelps, How arousal modulates memory: Disentangling the effects of attention and retention, Cogn. Affect. Behav. Neurosci. 4 (2004) 294–306. doi:10.3758/CABN.4.3.294.

[29] T. Sharot, A.P. Yonelinas, Differential time-dependent effects of emotion on

recollective experience and memory for contextual information, Cognition. 106 (2008) 538–547. doi:10.1016/j.cognition.2007.03.002.

[30] J. Han, Y. Zhu, S. Li, J. Zhang, X. Cheng, O. Van den Bergh, K.P. Van de Woestijne, The language of medically unexplained dyspnea, Chest. 133 (2008) 961–968. doi:10.1378/chest.07-2179.

[31] D.J.C. Read, A clinical method for assessing the ventilatory response to carbon dioxide, Australas. Ann. Med. 16 (1967) 20–32.

[32] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fourth ed., American Psychiatric Publishing, Washington DC: Arlington, VA, 2000.

[33] C.J. Wientjes, P. Grossman, Overreactivity of the psyche or the soma? Interindividual associations between psychosomatic symptoms, anxiety, heart rate, and end-tidal partial carbon dioxide pressure, Psychosom. Med. 56 (1994) 533–540. doi:10.1097/00006842-199411000-00009.

[34] U. Engelen, S. De Peuter, A. Victoir, I. Van Diest, O. Van den Bergh, Verdere validering van de Positive and Negative Affect Schedule (PANAS) en vergelijking van twee nederlandstalige versies, Gedrag Gezond. 34 (2006) 89–102.

[35] D. Watson, L.A. Clark, A. Tellegen, Development and validation of brief measures of positive and negative affect: The PANAS scales, J. Pers. Soc. Psychol. 54 (1988) 1063–1070. doi:10.1037/0022-3514.54.6.1063.

[36] A.J.W. Van der Does, Handleiding bij de Nederlandse bewerking van de BDI-II [Manual of the Dutch version of the BDI-II], The Psychological Corporation/Swets Test Publishers, San Antonio, Texas/Lisse, The Netherlands, 2002.

[37] K. Bogaerts, A. Millen, W. Li, S. De Peuter, I. Van Diest, E. Vlemincx, S. Fannes, O. Van den Bergh, High symptom reporters are less interoceptively accurate in a symptom-related context, J. Psychosom. Res. 65 (2008) 417–424. doi:10.1016/j.jpsychores.2008.03.019.

[38] G. Borg, Ratings of perceived exertion and heart rates during short-term cycle exercise and their use in a new cycling strength test., Int. J. Sports Med. 3 (1982) 153–158. doi:10.1055/s-2008-1026080.

[39] K.J. Preacher, A.F. Hayes, Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models, Behav. Res. Methods. 40 (2008) 879–891. doi:10.3758/BRM.40.3.879.

[40] A.F. Hayes, Introduction to mediation, moderation, and conditional process analysis: A regression-based approach, The Guilford Press, New York, 2013.

[41] K. Bogaerts, L. Van Eylen, W. Li, J. Bresseleers, I. Van Diest, S. De Peuter, L. Stans, M. Decramer, O. Van den Bergh, Distorted symptom perception in patients with medically unexplained symptoms., J. Abnorm. Psychol. 119 (2010) 226–234. doi:10.1037/a0017780.

[42] L. Giske, L. Sandvik, C. Røe, Comparison of daily and weekly retrospectively reported pain intensity in patients with localized and generalized musculoskeletal pain, Eur. J. Pain. 14 (2010) 959–965. doi:10.1016/j.ejpain.2010.02.011.

[43] J.J.E. Broderick, J.J.E. Schwartz, G. Vikingstad, M. Pribbernow, S. Grossman, A.A. Stone, The accuracy of pain and fatigue items across different reporting periods, Pain. 139 (2008) 146–157. doi:10.1016/j.pain.2008.03.024.

[44] R.N. Jamison, S.A. Raymond, E.A. Slawsby, G.J. McHugo, J.C. Baird, Pain assessment in patients with low back pain: Comparison of weekly recall and

momentary electronic data, J. Pain. 7 (2006) 192–199. doi:10.1016/j.jpain.2005.10.006.

[45] I. Van Diest, S. De Peuter, A. Eertmans, K. Bogaerts, A. Victoir, O. Van den Bergh, Negative affectivity and enhanced symptom reports: Differentiating between symptoms in men and women, Soc. Sci. Med. 61 (2005) 1835–1845. doi:10.1016/j.socscimed.2005.03.031.

[46] C.M.T. Gijsbers van Wijk, H. Huisman, A.M. Kolk, Gender differences in physical symptoms and illness behavior, Soc. Sci. Med. 49 (1999) 1061–1074. doi:10.1016/S0277-9536(99)00196-3.

[47] L. Wan, I. Van Diest, S. De Peuter, K. Bogaerts, O. Van den Bergh, Repeated breathlessness experiences induced by hypercapnia: differential effects on intensity and unpleasantness., Chest. 135 (2009) 455–61. doi:10.1378/chest.08-1226.

[48] A.J. Barsky, H.M. Peekna, J.F. Borus, Somatic symptom reporting in women and men, J. Gen. Intern. Med. 16 (2001) 266–275. doi:10.1046/j.1525-1497.2001.016004266.x.

[49] A. Aamland, K. Malterud, E.L. Werner, Patients with persistent medically unexplained physical symptoms: a descriptive study from Norwegian general practice, BMC Fam. Pract. 15 (2014) 107. doi:10.1186/1471-2296-15-107.

[50] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fifth ed., American Psychiatric Publishing, Washington, DC: Arlington, VA, 2013.

[51] A. Hovasapian, L.J. Levine, Reappraisal mitigates overestimation of remembered pain in anxious individuals, Cogn. Emot. 30 (2016) 1222–1231. doi:10.1080/02699931.2015.1049937.

Table 1. Group comparisons of demographic and personality trait characteristics.

Variable	Patients (n = 22)	Controls (n = 22)	Statistics
Age, mean (SD)	36.86 (9.58)	37.59 (9.94)	$t(42) = -.25$, $p = .81$
BMI (kg/m^2)	23.53 (4.05)	22.07 (2.38)	$t(33.93) = 1.46$, $p = .15$
Working, n (%)	18 (81.8)	18 (81.8)	$\chi^2(1, n = 44) = 0$, $p = 1.00$
Marital status, n (%)			$\chi^2(3, n = 44) = 1.35$, $p = .72$
Married or cohabiting	15 (68.2)	14 (63.6)	
Single	4 (18.2)	5 (22.7)	
Divorced	2 (9.1)	3 (13.6)	
Widow	1 (4.5)	0 (0)	
Education level, n (%)			$\chi^2(2, n = 44) = 1.93$, $p = .38$
High school	8 (36.4)	4 (18.2)	
College	7 (31.8)	10 (45.5)	
University	7 (31.8)	8 (36.4)	
NA	29.45 (7.40)	16.14 (4.63)	$t(42) = 7.16$, $p < .001$
BDI-II	19.32 (9.41)	4.50 (4.48)	$t(30.06) = 6.67$, $p < .001$
CSD	115.50 (17.51)	62.68 (7.82)	$t(29.05) = 12.92$, $p < .001$

Note. SD = standard deviation; BMI = Body Mass Index; NA = Negative Affectivity; BDI-II = Beck Depression Inventory; CSD = Checklist for Symptoms in Daily Life.

Table 2. Number (and percentages) of participants per group (controls and patients) who preferred the short or the long trial on each of the forced-choice questions assessing the peak-end effect.

Question	*df*, χ^2	Short trial	Long trial	No difference	*df*, χ^2
PE-Preference1: Which trial would you prefer to repeat tomorrow?					
Controls	1, 0.73	9 (40.9)	13 (59.1)		1, .10
Patients	1, 1.64	8 (36.4)	14 (63.6)		
PE-Preference2: Which trial would you pick for today's third trial?					
Controls	1, 0.73	9 (40.9)	13 (59.1)		1, .09
Patients	1, 0.18	10 (45.5)	12 (54.5)		
PE-Discomfort: Which trial caused greatest discomfort?					
Controls	1, 8.91**	18 (81.8)	4 (18.2)		1, 4.96*
Patients	1, 0.00	11 (50.0)	11 (50.0)		
PE-Duration: Which trial lasted longer?					
Controls	2, 12.64**	2 (9.1)	15 (68.2)	5 (22.7)	2, 2.09
Patients	2, 27.91***	1 (4.5)	19 (86.4)	2 (9.1)	
PE-Max Discomfort: Which trial caused greatest distress at peak?					
Controls	1, 4.55*	16 (72.7)	6 (27.3)		1, 1.57
Patients	1, .18	12 (54.5)	10 (45.5)		
PE-Max Dyspnea: Which trial caused the greatest amount of dyspnea at peak?					
Controls	1, 2.91[a]	15 (68.2)	7 (31.8)		1, 2.32
Patients	1, .18	10 (45.5)	12 (54.5)		

Note. Significant χ^2 values in the first column indicate the within group differences in the choice for the short versus long trial. Significant χ^2 values in the last column indicate the between group differences in the choice for the short versus long trial. For each of the questions, participants could choose between the first and the second trial, except for the PE-Duration, which included the option "no difference".

[a] $p < .10$, * $p < .05$,** $p < .01$

Table 3. Means (SDs) for state symptoms, state negative affect (NA), and state anxiety in patient (n = 22) and control (n = 22) groups.

		Trial			Statistics			
Variable	Group	Baseline	Short trial	Long trial	Significant effects	F-test (df)	p	η_p^2
State symptoms	Patients	72.64 (16.11)[a]	89.36 (26.96)[b]	86.09 (25.36)[b]	Trial	15.28 (1.33, 53.02)	<.001	.28
	Controls	51.05 (4.40)[c]	62.36 (12.23)[d]	61.77 (12.02)[d]	Group	28.96 (1,40)	<.001	.42
State NA	Patients	18.05 (5.00)[a]	18.77 (6.14)[a]	18.59 (5.85)[a]	Group	34.97 (1,40)	<.001	.47
	Controls	12.45 (2.69)[b]	12.55 (2.13)[b]	12.32 (1.86)[b]				
State anxiety	Patients	2.59 (1.62)[a]	4.73 (2.41)[b]	4.41(2.02)[b]	Trial	23.85 (1.48, 59.08)	<.001	.37
	Controls	1.55 (.96)[c]	2.50 (1.50)[a]	2.27 (1.24)[ac]	Group	17.54 (1, 40)	<.001	.31
					Trial × Group	3.79 (1.48, 59.08)	.04	.09

Note. Means with different superscripts are significantly different at $p < .05$.

Figure captions

Figure 1. Study procedure. (1-column fitting image)

Figure 2. Mean values and standard errors of concurrent dyspnea (0-100), minute ventilation, and fractional end-tidal concentration of CO_2 ($FetCO_2$) for controls and patients with MUD in baseline, rebreathing, and recovery phase for the short (left) and the long trial (right). Whiskers denote standard errors. (1-column fitting image)

Figure 3. Mean averaged concurrent and retrospective dyspnea ratings (0-100) for controls and patients with MUD. Whiskers denote standard errors. (1-column fitting image)

Figure 4. Multiple-mediator models for short (left) and long dyspnea trials (right). The panels show direct and indirect effects of a group (patients/controls) on the retrospective dyspnea ratings, mediated by state anxiety and concurrent dyspnea ratings. The model coefficients are reported in unstandardized form. (1.5-column fitting image)

Figure 1.

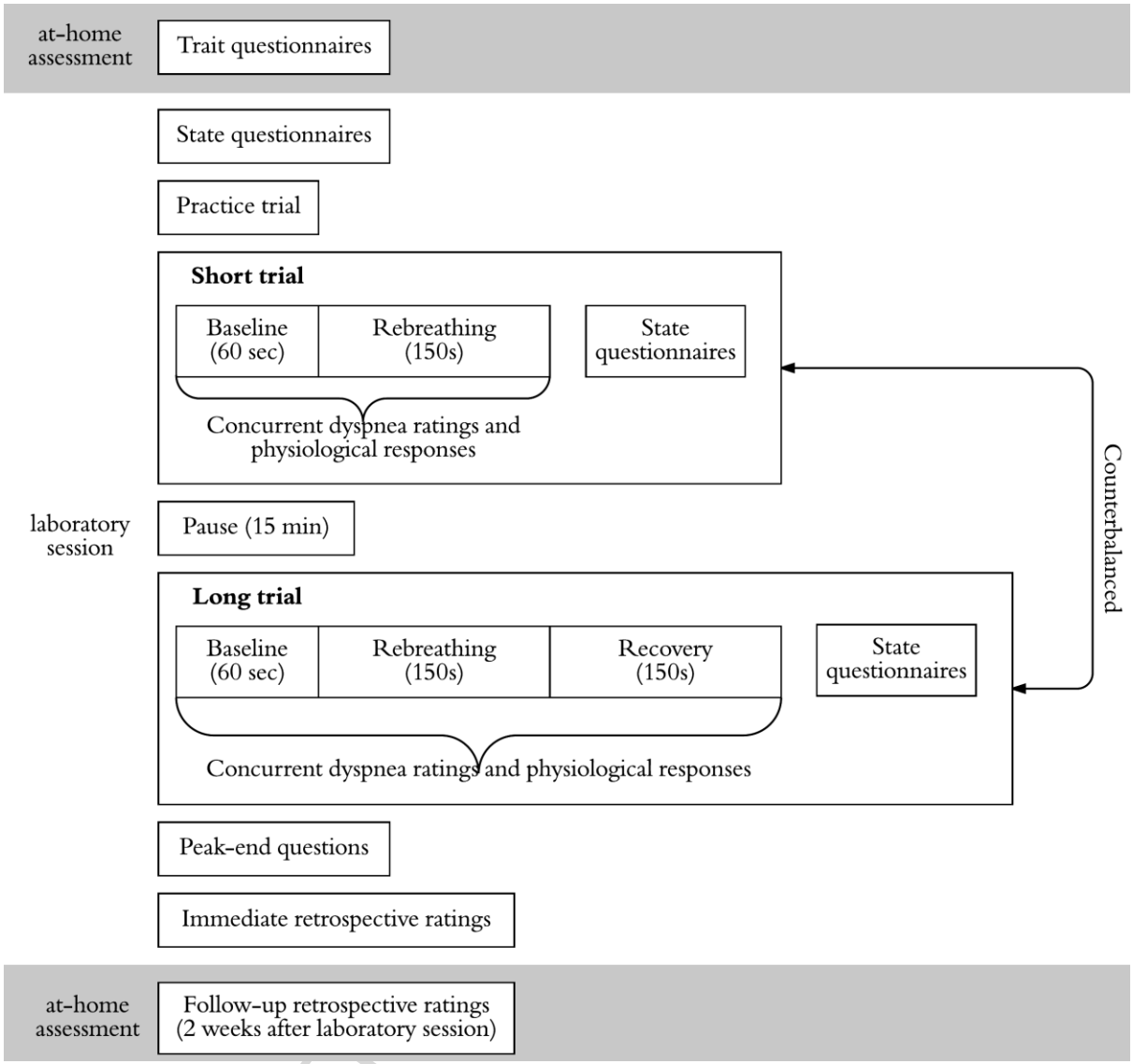


Figure 2.

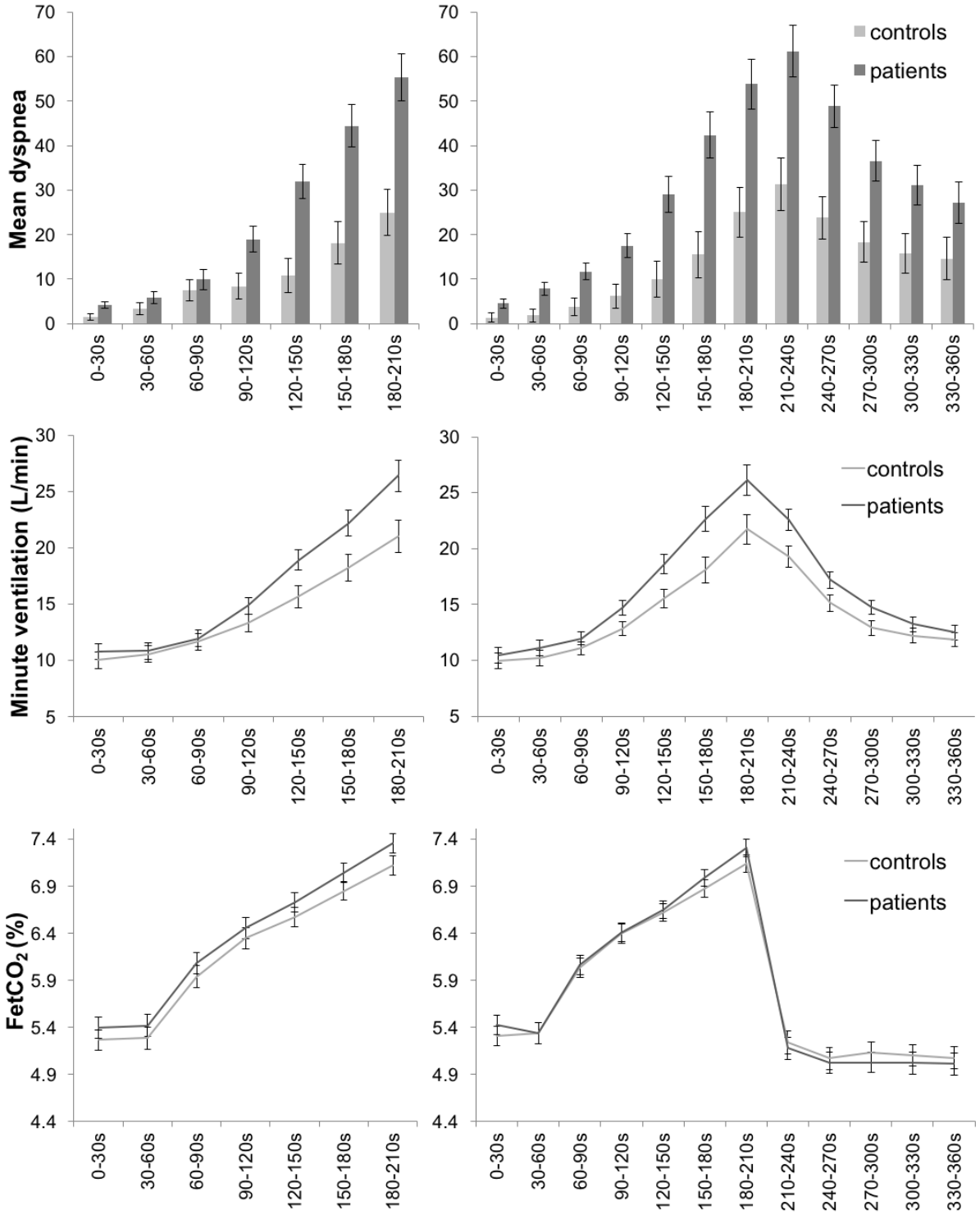


Figure 3.

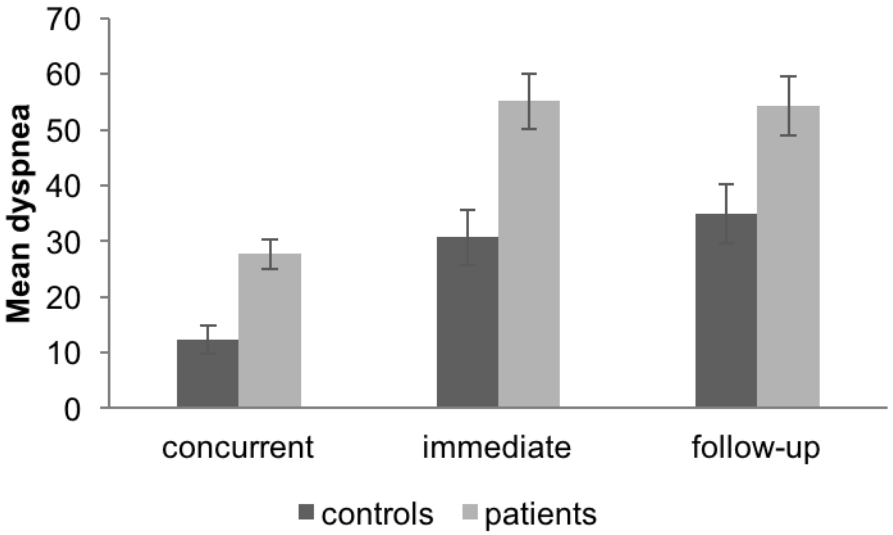
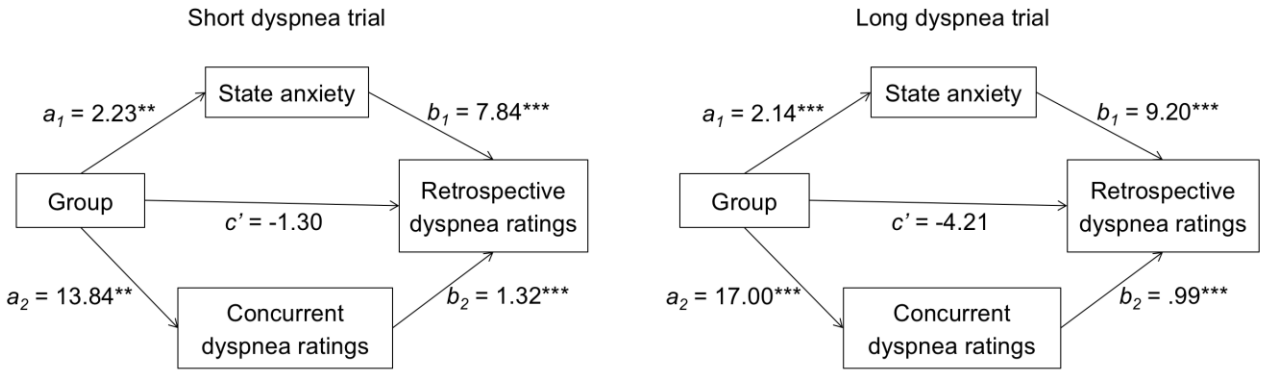


Figure 4.



Note: $^*p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Highlights

- Patients with MUS respond with higher anxiety and dyspnea to a rebreathing test.
- Affective state during the symptom episode mediates retrospective symptom reports.
- Retrospective dyspnea ratings were higher than the average of concurrent ratings.
- Retrospective dyspnea ratings did not increase over a 2-week period.
- Patients with MUS did not show a peak-end effect.