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Perception of induced dyspnea in fibromyalgia and chronic fatigue syndrome

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ABSTRACT

Objective: Dyspnea perception is distorted in patients with medically unexplained dyspnea. The goals of this study were 1) to replicate these results in patients with fibromyalgia and/or chronic fatigue syndrome (CFS), and 2) to investigate predictors of distorted symptom perception within the patient group, with a focus on negative affectivity (NA), psychiatric comorbidity and somatic symptom severity.

Methods: Seventy-three patients diagnosed with fibromyalgia and/or CFS and 38 healthy controls (HC) completed a rebreathing paradigm, consisting of a baseline (60 s of room air), a rebreathing phase (150 s, gradually increasing ventilation, partial pressure of CO_2 in the blood, and self-reported dyspnea), and a recovery phase (150 s of room air). Dyspnea, respiratory flow and $FetCO_2$ levels were measured continuously.

Results: Patients reported more dyspnea than HC in the recovery phase ($p = 0.039$), but no differences between patients and HC were found in the baseline ($p = 0.07$) or rebreathing phase ($p = 0.17$). No significant differences between patients and HC were found in physiological reactivity. Within the patient group, the effect in the recovery phase was predicted by somatic symptom severity ($p = 0.046$), but not by negative affectivity or by the number of psychiatric comorbidities.

Conclusion: This study extended earlier findings in patients with medically unexplained dyspnea to patients with fibromyalgia and CFS. This suggests that altered symptom perception is a non-symptom-specific mechanism underlying functional somatic syndromes in general, particularly in patients with high levels of somatic symptom severity. The results are discussed in a predictive coding framework of symptom perception.

1. Introduction

About 40–49% of patients in primary care present with medically unexplained symptoms (MUS; symptoms not corresponding to bodily dysfunction [1]). Some patients present with chronic MUS that are highly debilitating. Depending on the reported symptoms and the consulted medical specialty, different labels are used to describe the condition, like fibromyalgia, chronic fatigue syndrome (CFS), or medically unexplained dyspnea. Combined, these types of syndromes are referred to as functional somatic syndromes (FSS).

It has been proposed that FSS are at least partly a disorder of symptom perception [2,3]. Symptom perception is influenced by (bottom-up) somatic sensations and (top-down) attentional, affective and memory processes [4]. Because the relative contribution of these processes to the actual symptoms varies between and within persons, so does the correspondence between afferent input and reported symptoms. It has been proposed that FSS represent one extreme end of this continuum: afferent input is processed in such a way that eventually there is little correspondence between the afferent input and the subjective experience of symptoms [3,5].

Critical variables moderating the within-person correspondence between induced physiological changes and symptom reports have been demonstrated in experimental studies using a rebreathing paradigm. In these experiments, participants breathed through a circuitry

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either connected to room air or to a bag initially filled with 5% CO_2 and 95% oxygen, causing gradual increase in ventilation, partial (arterial) CO_2 pressure and self-reported feelings of dyspnea (air hunger). Concealed from the participant, participants switch to room air breathing after 150 s of rebreathing allowing recovery. These studies have shown that healthy high habitual symptom reporters and patients with medically unexplained dyspnea show a reduced within-subject correspondence between induced physiological changes and perception thereof, compared to healthy controls [6–8]. However, these differences were found only after switching to room air breathing (recovery), and not during rebreathing. In addition, this reduced "body-symptom" correspondence only emerges when participants rate "breathlessness" and not when they rate "faster/deeper breathing". This pattern of results shows that when the afferent input is weak (recovery) and the context generates anticipation of symptoms, the correspondence between self-reported symptoms and induced physiological changes drops significantly in FSS compared to HC.

So far, this paradigm has only been administered in FSS patients with medically unexplained dyspnea [8]. Given the debate on the specificity of different FSS [9–11] and the hypothesis that the deficit in symptom perception underlies FSS in general [3], the first goal of this study was to investigate whether results found in patients with medically unexplained dyspnea [8] extend to patients with fibromyalgia and CFS. The second goal of this study was to look for predictors of distorted symptom perception within the patient group. We therefore chose to investigate the effects of three variables that are related to symptom reporting, symptom severity and quality of life within the fibromyalgia/CFS patient group: negative affectivity (NA), psychiatric comorbidity and somatic symptom severity [12–16]. Somatic symptom severity was measured with the somatic symptom subscale of the Patient Health Questionnaire [17].

2. Methods

2.1. Participants

Patients were recruited through the Psychiatry Departments of East Limburg Hospital (Genk) and University Hospital Gasthuisberg (Leuven), and through a Rheumatology Center (Genk). Only patients with a doctor-based diagnosis for CFS and/or fibromyalgia were included. After inclusion, participants additionally filled out a questionnaire checking the 1994 CDC criteria of CFS [18] and 2010 ACR criteria for fibromyalgia [19]. Exclusion criteria for patients were a body mass index > 35, pregnancy, alcohol- or drug dependence, anorexia or bulimia nervosa, (history of) psychosis and chronic cardiovascular, respiratory or neurological disorders. Healthy controls (HC) were recruited through local advertisement. HC were excluded if they had any chronic medical disorders or (history of) psychiatric disorders. In order to investigate predictors within the patient group, we recruited twice as many patients as HC. HC were recruited by means of frequency matching, so that the distribution of age and gender was similar in both groups. All participants provided written informed consent. The study was approved by the Medical Ethics Committees of University Hospital Gasthuisberg, Leuven and East Limburg Hospital, Genk.

2.2. Design

This study was part of a larger study involving four experimental paradigms administered to the same participants, aiming to investigate symptom perception in fibromyalgia and CFS. Participants went through a psychiatric diagnostic interview by telephone, filled out an online questionnaire battery and participated in a single test session in either the University Hospital of Leuven or in Hospital ZOL. This test session consisted of 1) a non-invasive baseline measurement of physiological parameters, 2) a picture viewing paradigm, in which patients viewed a series of negative, positive and neutral pictures, 3) a rebreathing paradigm, 4) a conditioning paradigm with a fearful face and unpleasant sound as negative reinforcement and 5) a conditioned pain modulation paradigm in which participants received painful electrocutaneous stimulation. Only the results of the rebreathing paradigm are reported here. Detailed methods and results of the picture viewing paradigm and conditioned pain modulation paradigm are reported elsewhere [20,21].

2.3. Self-report measures

Negative affectivity was measured with the negative affect subscale of the trait Positive and Negative Affect Schedule (PANAS; [22]). Respondents indicate on a five-point scale (1: very slight - 5: very much) to what extent they experience ten positive and ten negative feelings in daily life.

Somatic symptom severity was measured with the somatic symptom scale of the Patient Health Questionnaire (PHQ-15: 17). Respondents indicate to what extent they were bothered by 15 common somatic symptoms in the past two weeks on a three-point scale (0: not bothered at all - 2: bothered a lot).

Dyspnea during the rebreathing test was measured with a 100-point numeric rating scale. Labels next to the scale were: no dyspnea (0), barely noticeable [5], very slight [10], slight [20], moderate [30], rather strong (40), strong (50), very strong (60–80), very very strong (90), unbearable (100). Dyspnea ratings were measured continuously, sampled at 10 Hz and stored on a personal computer.

Psychiatric comorbidity was assessed with the MINI International Neuropsychiatric Interview [23,24], which is based on the DSM-IV criteria for psychiatric disorders and checks, among others, for the presence of a depressive episode, (hypo)mania, panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, generalized anxiety disorder and somatization disorder. A psychiatric comorbidity score was made and patients were allocated to one of four categories (no, 1, 2 and 3 or more comorbid psychiatric disorders).

2.4. Apparatuses and physiological recordings

The standard rebreathing paradigm [25] was used. Participants wore a nose clip and breathed through a mouthpiece. A Y-valve connected the mouthpiece to either room air or the rebreathing bag filled with a gas mixture consisting of 95% oxygen and 5% carbon dioxide (CO_2). The experimenter could switch the breathing circuit to one of the two arms of the Y-valve. Breathing through the rebreathing bag causes a progressive increase of CO_2 levels in the blood, self-reported dyspnea and respiratory flow. Airflow was measured with a pneumotachograph (CD15, Validyne, Northridge, CA in ZOL; PNT 4813, Hans Rudolph, Shawnee, KA in Leuven). Fractional end-tidal CO_2 ($FetCO_2$) was measured with a capnograph (POET RC, Criticare Systems Inc., Waukesha, WI in ZOL; Capnogard, Novametrix, Wallingford, CT, USA in Leuven). $FetCO_2$ levels and respiratory flow were visually inspected and processed breath by breath with MatLab R2015a (Mathworks Inc, Massachusetts, USA). To correct for equipment differences, $FetCO_2$ was defined as the relative change in $FetCO_2$ compared to right before the rebreathing test. To quantify respiratory flow, inspiratory time (Ti), expiratory time (Te), inspiratory volume (Vi), and expiratory volume (Ve) were extracted for every breath. Minute Ventilation was calculated per breath with the following formula: respiratory rate (RR) × Vt, with $RR = 60/(Ti + Te)$ and $Vt = (Vi + Ve)/2$.

2.5. Procedure

Right before the rebreathing test, respiratory parameters were measured for 30 s without the rating scale. The rebreathing test consisted of 60 s of breathing room air (= baseline phase), 150 s of rebreathing (= rebreathing phase), and 150 s of breathing room air