Journal of Psychiatric Research 43 (2009) 634–641

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Changes in respiration mediate changes in fear of bodily sensations in panic disorder

Alicia E. Meuret [a,*], David Rosenfield [a], Stefan G. Hofmann [b], Michael K. Suvak [b], Walton T. Roth [c]

[a] Department of Psychology, Southern Methodist University, Dallas, TX, United States
[b] Department of Psychology, Boston University, Boston, MA, United States
[c] Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine Stanford University, Palo Alto, CA, United States

ARTICLE INFO

Article history:
Received 15 June 2008
Received in revised form 15 August 2008
Accepted 19 August 2008
Available online xxxx

Keywords:
Carbon dioxide
Anxiety sensitivity
Breathing therapy
Mediation
Panic disorder
Respiratory physiology

ABSTRACT

The purpose of the study was to examine whether changes in pCO_2 mediate changes in fear of bodily sensation (as indexed by anxiety sensitivity) in a bio-behavioral treatment for panic disorder that targets changes in end-tidal pCO_2. Thirty-five panic patients underwent 4 weeks of capnometry-assisted breathing training targeting respiratorydysregulation. Longitudinal mediation analyses of the changes in fear of bodily symptoms over time demonstrated that pCO_2, but not respiration rate, was a partial mediator of the changes in anxiety sensitivity. Results were supported by cross lag panel analyses, which indicated that earlier pCO_2 levels predicted later levels of anxiety sensitivity, but not vice versa. PCO_2 changes also led to changes in respiration rate, questioning the importance of respiration rate in breathing training.

The results provide little support for changes in fear of bodily sensations leading to changes in respiration, but rather suggest that breathing training targeting pCO_2 reduced fear of bodily sensations in panic disorder.

1. Introduction

Abnormalities that may maintain panic disorder (PD) include low levels of carbon dioxide partial pressure (pCO_2), which is the defining characteristic of hyperventilation, instabilities in blood gas regulation, and oversensitivities of chemoreceptors (oversensitive "suffocation alarm system"; Klein, 1993). There are several experimental studies that support this association: lowering pCO_2 into the hypocapnic range or increasing pCO_2 into the hypercapnic range often results in panic-like symptoms in PD patients (Dager et al., 1995; Maddock and Carter, 1991; Wilhelm et al., 2001; Gorman et al., 2004; but see Beck et al., 1999). Furthermore, sustained hypocapnic levels have been observed in PD (Papp et al., 1995; Salkovskis et al., 1986; Meuret et al., 2008; but see also, Garssen et al., 1996).

The nature of the pCO_2 dysregulation has been outlined in two theories of PD. Klein (1993) postulated a hypersensitive suffocation alarm system that triggers panic attacks when pCO_2 rises; consequently PD patients keep levels of pCO_2 low. Ley (1985a) emphasized the panicogenic effects of acute hyperventilation by which a vicious circle of chronic and acute levels of hypocapnia (low pCO_2 levels) causes feared bodily sensations (in particular, dyspnea), which leads to more hyperventilation. This cycle may ultimately culminate in full-blown panic (Ley, 1985a,b, 1987).

If respiratory dysregulation is a central feature of PD, then interventions specifically targeting respiratory dysregulation may be effective in treating it. We tested this idea by devising a capnometry-assisted breathing training therapy that uses immediate feedback to teach patients how to raise their pCO_2 over a series of training and practice sessions. The treatment led to sustained increases in pCO_2 levels and decreases in respiratory rate and was successful in substantially reducing panic severity and frequency (Meuret et al., 2008). However, the mechanism by which this treatment worked remains unknown.

The purpose of this study was to examine the causal and temporal relationships between pCO_2, respiration rate, and self-reported changes in fearful symptom interpretation in a respiratory treatment for PD. We chose anxiety sensitivity (AS) as a measure of fear of bodily symptoms. This construct is conceptualized as a disposition that determines the tendency to respond fearfully to anxiety symptoms such as heart racing or shortness of breath (Reiss and McNally, 1985). These (feared) physical symptoms are closely related to symptoms triggered by hypocapnia.

We predicted that by reducing hypocapnia, a reduction of fear of bodily sensations, and thereby the fearful interpretation of those symptoms, would be achieved. Thus, changes in pCO_2 would mediate and precede changes in fearful interpretation of symptoms measured by the anxiety sensitivity index (ASI).

* Corresponding author. Address: Department of Psychology, Southern Methodist University, P.O. Box 750442, Dallas, TX 75275, United States. Tel.: +1 214 7683422; fax: +1 214 7683910.
E-mail address: ameuret@smu.edu (A.E. Meuret).

0022-3956/$34.00 © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jpsychires.2008.08.003

2. Method

2.1. Study design

The data set for the present analyses was part of a randomized controlled trial investigating the efficacy of capnometry-assisted breathing training for treatment of panic disorder. While the overall outcome of the treatment was reported elsewhere (Meuret et al., 2008), we here analyze the temporal relationships of pCO_2 and anxiety sensitivity changes across the course of treatment. A more detailed description of the methods is provided in our prior report.

2.2. Participants

The sample consisted of 35 patients with a principle DSM-IV (American Psychiatric Association, 1994) Axis I diagnosis of PD with or without agoraphobia. Patients met the following inclusion criteria: (a) ages 18–60, (b) if taking psychotropic medication, on a stable dose for at least 3 months prior to treatment with an agreement not to change dosage until after the 2-month follow-up, unless necessary, and (c) no evidence of organic mental disorder, suicide intention, schizophrenia, alcohol or drug dependence, cardiovascular disease, pulmonary disease, epilepsy or pregnancy.

The final sample consisted of 22 females and 13 males. Thirty-one were White, one African–American, two Hispanic and two were Asian. On average, participants were 41 years old (SD: 8.6), with a duration of the PD averaging 9 years (range 0.5–32). Fifty-four percent reported some degree of agoraphobic avoidance. Forty-nine percent had at least one secondary current Axis I diagnosis. Of these, all were diagnosed with at least one additional anxiety disorder (48% specific phobia, 30% social anxiety disorder, 22% generalized anxiety disorder). Fourteen percent were diagnosed with an additional current diagnosis of major depressive disorder and 14% were diagnosed with both anxiety and mood disorder. Thirty-one percent of the patients were taking a stable dose of psychotropic medications (benzodiazepines ($n = 6$), antidepressants ($n = 4$), beta-blockers ($n = 1$) and other anxiolytics ($n = 1$)). Diagnosis was obtained using the structured clinical interview for DSM-IV patient edition (First et al., 1994). Interrater reliability was high for all Axis I diagnoses and PD ($\kappa = .83$, $\kappa = 1.00$).

This study was approved by the Institutional Review Board at Stanford University and all subjects signed written informed consent before entering the study.

2.3. Treatment

The treatment was designed to increase self-monitored end-tidal pCO_2 and to reduce respiration rate (RR) by means of breathing exercises. It consisted of five weekly 1 h treatment sessions. During these sessions, patients were educated about the effects of hyperventilation and respiratory dysregulation on panic symptoms. They were taught how to increase self-monitored end-tidal pCO_2, and to reduce RR and respiratory instability with the goal being to change hypocapnic levels of pCO_2 (hypocapnic range as defined by $pCO_2 < 35$ mm Hg; Oakes, 1996), thereby changing symptoms and fear of these symptoms associated with PD. No other instructions or techniques were discussed or used (e.g., cognitive restructuring and in vivo exposure).

Highly structured home exercises, using a handheld capnometry device in addition to pacing tones, were a central component of this treatment. The instrument analyses and displays breath-by-breath end-tidal pCO_2 (in mm Hg) and RR (in breaths/min), and records them along with the time and date (Meuret et al., 2005a,b). In addition to the visual feedback of the capnometer, patients were provided audio tapes to guide their pace of breathing during the exercises. For more details see Meuret et al. (2001, 2004, 2008).

2.4. Assessments

Fear of bodily symptoms and physiological data (pCO_2 and RR) were collected at five time points: pretreatment, sessions two, three and four, and at posttreatment. The measures of interest were assessed as described below.

Fear of bodily symptoms was assessed with the anxiety sensitivity index (ASI). The 16 items comprising the ASI (Reiss et al., 1986) assess a set of beliefs that unexplained somatic sensations are dangerous and may cause deleterious physical, psychological, or social consequences that go beyond any immediate physical discomfort. Items are rated on a scale from 0 (very little) to 4 (very much). Anxiety sensitivity is conceptualized as a dispositional and dimensional construct that determines the tendency to respond fearfully to anxiety symptoms (McNally, 1994; Reiss, 1991; Reiss and McNally, 1985; Taylor et al., 1992)[1] The ASI was administered at pretreatment and posttreatment, and at the beginning of each treatment session. Mean ASI scores were 30.7 at pretreatment and 17.0 at posttreatment.

Baseline end-tidal pCO_2 (pCO_2). End-tidal pCO_2 (mm Hg) was collected and stored by the capnometry device to measure treatment compliance and progress. Patients completed an average of 47.6 (91.3%) of the 52 homework exercises assigned over the course of the four week treatment. Baseline pCO_2 levels were obtained at pretreatment and from the first homework exercise after each treatment session, except posttreatment, for which we used the last exercise before the posttreatment assessment (there were no exercises after posttreatment assessment). This portable capnometer technique has been demonstrated to meet international accuracy standards (Biedler et al., 2003). Baseline pCO_2 changed from hypocapnic levels at pretreatment (32.3 mm Hg) to normocapnic levels are posttreatment (38.2 mm Hg).

Baseline respiration rate (RR). Respiration rate was computed and recorded at the same assessment times as pCO_2. While the treatment goal for pCO_2 was to achieve and maintain normocapnic levels, the goal for RR was to gradually reduce the rate to lower levels. The pacing tones were set to correspond to an RR of 13 breaths per minute in the first week, and rates of 11, 9 and 6 breaths per minute in successive following weeks. Baseline RR was 12.4 breath/minute at pretreatment and 11.4 breath/minute at posttreatment.

3. Data analysis

The longitudinal nature of our design produced a multilevel, or nested, data structure. The lower level, or level-1, data consisted of the repeated measures that were collected at each treatment session (i.e., ASI, pCO_2 level, RR). The level-1 data were nested within upper level, or level-2, units (i.e., participants). Thus, our data structure was comprised of repeated measures (level-1 data) nested within individuals (level-2 data).

The focus of this longitudinal approach to the data analysis is to examine how an individual's score on a variable changes as a function of time. Thus, growth curves over time were calculated for

[1] Some psychometric studies of the ASI support a multidimensional and hierarchical factor structure consisting of 3 lower order and 1 higher order factor (e.g., Zinbarg et al., 1997), whereas other studies support a taxonic latent class structure composed of 2 dimensional types of anxiety sensitivity (e.g., Bernstein et al., 2007). To be consistent with the majority of experimental studies that utilized the ASI (see Taylor, 1999, for a review), and given the conceptual definition of the construct, we decided to examine anxiety sensitivity as a unidimensional construct.