

Effects of Capnometry-Assisted Breathing Therapy on Symptoms and Respiration in Panic Disorder

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I. Introduction and Overview

This report outlines theoretical background, methods and results of Capnometry-Assisted Breathing, a novel behavioral intervention to treat panic disorder. The studies presented in this doctoral thesis were conducted from 1999 until 2003 at the Laboratory of Clinical Psychopharmacology and Psychophysiology, Palo Alto Veterans Administration Health Care System in association with the Stanford University Department of Psychiatry and Behavioral Sciences under the supervision of Prof. Walton T. Roth.

Breathing training has been discussed for some time as an intervention to reduce hyperventilation-produced symptoms in panic disorder. Although the theoretical implications with respect to the regulation of breathing and the role of hypocapnea in triggering anxiety are straightforward, clinical research has suffered from conceptual and methodological weaknesses. Voluntary hyperventilation has been employed in various ways in panic disorder treatment, but its theoretical and practical implications for therapy, as well as its actual effect on patients has rarely been reflected.

In this doctoral project, a method for altering $p\text{CO}_2$ -levels was developed using feedback from a small hand-held capnometry device. In a 4-week therapy that comprised 5 sessions of education and training as well as twice-daily home-based breathing exercises panic patients systematically increased their $p\text{CO}_2$ -levels by breathing slow and shallow using pacing tones as guidance. Panic frequency and severity, global impairment, agoraphobic avoidance, anxiety sensitivity, depression, and response to voluntary hyperventilation were measured before and after training, as well as 3 and 12 months following training. Compared to a waiting control group, panic patients of the intervention group showed increases in $p\text{CO}_2$ -levels and marked reductions in panic symptoms and anxiety. They also managed to return faster to normal $p\text{CO}_2$ levels following voluntary hyperventilation. These improvements were sustained at 3- and 12-months follow-up. In addition to the results from the clinical trial, an individual case is reported that illustrates the therapeutic techniques and the course of the treatment. In conclusion, $p\text{CO}_2$ -biofeedback assisted breathing training is a theoretically well-funded and clinically effective behavioral treatment for panic disorder.

Breathing Training for Treating Panic Disorder

Useful Intervention or Impediment?

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Breathing training (BT) is commonly used for treatment of panic disorder. We identified nine studies that reported the outcome of BT. Overall, the published studies of BT are not sufficiently compelling to allow an unequivocal judgment of whether such techniques are beneficial. This article discusses problems with the underlying rationale, study design, and techniques used in BT, and it identifies factors that may have determined therapy outcomes. The idea that hypocapnia and respiratory irregularities are underlying factors in the development of panic implies that these factors should be monitored physiologically throughout therapy. Techniques taught in BT must take account of respiration rate and tidal volume in the regulation of blood gases ($p\text{CO}_2$). More studies are needed that are designed to measure the efficacy of BT using an adequate rationale and methodology. Claims that BT should be rejected in favor of cognitive or other forms of intervention are premature.

Keywords: *panic disorder; breathing training; efficacy; hyperventilation; respiration*

For several decades, abnormalities in respiration have been postulated as an important factor in the development or maintenance of anxiety disorders (Lum, 1981). Consequently, training programs have been devised to modify presumably pathogenic breathing. Breathing training (BT), sometimes called *breathing retraining*, has thus become a major therapeutic strategy in the treatment of panic disorder. Its general aim has been to influence dysfunctional habitual breathing patterns through direct or indirect control of respiratory muscles to relieve anxiety and improve general health. BT has been both part of treatment packages (Barlow, 2001; Craske, Barlow, & Meadows, 2000; Telch et al., 1993; Zuercher-White, 1998) and the entire treatment for panic disorder (Clark, Salkovskis, & Chalkley, 1985; Rapee, 1985). Recently, however, whether BT really contributes has been questioned. BT has been called a “rational placebo” (Garssen, de Ruiter, & Van Dyck, 1992) and has been suspected of limiting improvement (Schmidt et al., 2000; Taylor, 2001) and even of being counterproductive in treating panic disorder because it provides a false safety aid (Craske, Rowe, Lewin, & Noriega-Dimitri, 1997; Schmidt et al., 2000). Despite such criticisms and the increasingly popular focus on irrational thinking in the treatment of panic disorder (Barlow, 1988; Clark, 1986), BT continues to be included in multi-component treatment packages. Part of the reason for this may be that “patients tend to attribute a lot of change to it” (Barlow, 1997, p. 36), although, in Barlow’s opinion, BT is a relatively small contributor to patient improvement.

The rationale of BT is almost always based on a hyperventilation theory of anxiety that assumes a central role for hypocapnia in panic symptom production (Ley, 1985, 1992), usually postulating a positive feedback loop between increasing anxiety and increasing hyperventilation. The cognitive expression of this loop was part of the original exposition of the catastrophic cognition theory of panic (Clark, 1986).

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Improvement occurs when patients implicitly, or explicitly as a part of cognitive restructuring, learn to reinterpret their physical symptoms of hyperventilation as normal physiological reactions rather than life-threatening events. BT also leads patients to believe that they have immediate control over the escalation of their panic symptoms; this belief, whether true or false, will generally inhibit anxiety and panic (Wolpe & Rowan, 1988).

In this article, we review the studies that had been designed to test the efficacy of BT in the treatment of panic disorder and critically examine the psychophysiological assumptions upon which BT is based, which determine what form it should take and its therapeutic potential. We evaluate studies using BT either as a sole component or as a treatment component that can be clearly separated from the other interventions. Studies where breathing techniques are inextricably confounded with other components such as exposure (de Beurs, Lange, van Dyck, & Koele, 1995) or cognitive restructuring (de Ruiter, Rijken, Garssen, & Kraaimaat, 1989) are not included in our evaluation, nor are studies where patients were diagnosed with “hyperventilation syndrome” rather than panic disorder or agoraphobia (Grossman, de Swart, & Defares, 1985; Han, Stegen, de Valck, Clement, & Van de Woestijne, 1996; van Doorn, Folgering, & Colla, 1982). Hyperventilation syndrome has been questioned as a diagnostic entity in recent years (Spinhoven, Onstein, Sterk, & le Haen-Versteijnen, 1993), and its exact relationship with panic disorder is uncertain.

METHOD

We performed a systematic, keyword-driven (*panic, breathing, respiration*) search using Medline and PsychInfo to identify potential studies for inclusion in our evaluation. In addition, we searched the reference sections of the articles and reviews that we located for additional sources. We limited ourselves to studies involving patients older than 18 years with a diagnosis of panic disorder with or without agoraphobia, and to studies published in peer-reviewed, English-language journals.

RESULTS

Nine studies were identified as using BT either alone or in combination with other treatment modules (Table 1). The design of these studies aimed to allow the effect of BT to be separated from that of other components. The BT treatment comprised one to five sessions over the course of 2 to 4 weeks. Two studies (Bonn, Readhead, & Timmons, 1984; Craske et al., 1997) used exposure treatment, two studies (Franklin, 1989; Schmidt et al., 2000) used waiting-list control groups, and one study (Hibbert & Chan, 1989) used a placebo treatment to evaluate the effectiveness of BT. Four studies (Clark et al., 1985; Meuret, Wilhelm, & Roth, 2001; Rapee, 1985; Salkovskis, Jones, & Clark, 1986) did not include control groups.

BT AS SOLE TREATMENT COMPONENT

Rapee (1985) reported the effectiveness of respiratory control on panic attacks in a single-case study. He treated a woman suffering from panic disorder without agoraphobia. Hyperventilation was explained to her as something that produced and maintained panic disorder. A voluntary hyperventilation challenge helped the patient to recognize the physiological effects of hyperventilation and to eliminate them by diaphragmatic breathing and reduction of her respiratory rate to seven breaths per minute. The patient was instructed to practice that kind of breathing twice a day for 10 minutes. Following BT, panic attack frequency and severity and fear of anxiety symptoms decreased considerably. A feeling of greater control over physical symptoms was thought to contribute to the modification of thoughts of catastrophes leading to panic.

In the same year, Clark and colleagues (1985) reported the results of a behavioral intervention using respiratory control. They tested the hypothesis that respiratory control treatment alone would produce substantial reductions in panic attack frequency and anxiety symptoms. Participants who experienced repeated panic attacks and responded positively to an initial hyperventilation challenge were

(text continues on p. xxx)

TABLE 1
Breathing Training (BT) Evaluation Studies

<i>Study</i>	<i>Duration of BT Only</i>	<i>Treatment Group (n)</i>	<i>Control Group (n)</i>	<i>Outcome Measures</i>	<i>Findings</i>
BT as sole component					
Rapee (1985)	3 sessions/4 weeks	1	—	Panic attack frequency, duration and severity, symptoms, anxiety	Decrease in panic attack frequency and severity, symptoms, anxiety
Clark, Salkovskis, & Chalkley (1985)	2 sessions/2 weeks	18	—	Panic attack frequency and severity, anxiety, depression	Reduction in panic attack frequency, self-reported anxiety and depression
Salkovskis, Jones, & Clark (1986)	4 sessions/4 weeks	9	—	Panic attack frequency and severity, anxiety, depression, pCO ₂	Reduction in panic attack frequency, self-reported anxiety and depression; increase of pCO ₂ to normal levels
Hibbert & Chan (1989)	2 sessions/2 weeks (plus 3 weeks of exposure in vivo)	21	Placebo treatment, 19	Panic attack frequency and severity, anxiety, depression	Self-reported measures of anxiety improved equally in treatment and placebo groups; at posttreatment, observer but not self-report ratings improved more with BT

(continued)

TABLE 1 (continued)

<i>Study</i>	<i>Duration of BT Only</i>	<i>Treatment Group (n)</i>	<i>Control Group (n)</i>	<i>Outcome Measures</i>	<i>Findings</i>
Meuret, Wilhelm, & Roth (2001)	5 sessions/4 weeks	4	—	Panic attack frequency and severity, perceived fear of symptoms, trait anxiety and depression, pCO ₂ , RR	PDSS global scores, ASI, BDI, and STAI-T decreased substantially from pretherapy to posttherapy and remained stable or declined further at FU; increase of pCO ₂ to normal levels through FU
<u>BT in addition to other components</u>					
Bonn. Readhead, & Timmons (1984)	2 sessions/2 weeks (plus 7 weekly sessions of in vivo Exposure)	7	EX only, 5	Mean resting breathing rate, global phobia score, somatic symptom score, agoraphobia score, panic attack frequency	BT in combination with exposure was at least as effective as EX alone but was superior at 6-month FU in terms of mean resting RR, global phobia score, somatic symptoms score, and preventing panic attacks
Franklin (1989)	1 session/4 weeks (compared to IIR, CM, and IR)	4	IR, CM, IR (within subjects), WL	Daily anxiety questionnaires, agoraphobic avoidance and anxiety, behavioral measures, global change	BT reduced panic attack frequency and severity and behavioral measures of agoraphobia

Craske, Rowe, Lewin, & Noriega-Dimitri (1997)	2 sessions/2 weeks (plus CR and EX: 12 sessions/12 weeks)	18	IEX (plus CR and EX), 20	Panic apprehension, panic fear and avoidance, agoraphobic fear and avoidance, general distress	IEX was more effective on certain measures than BT in combination with CR and EX
Schmidt et al. (2000)	2 sessions/2 weeks (with CBT: 12 session/12 weeks; CBT ± BT)	21	CBT without BT, WL, 24	Panic disorder severity and frequency, avoidance, anxiety symptoms, depression, disability	Active treatment groups improved similarly on the outcome measures compared to WL; patients in the CBT group without BT showed a trend for higher end-state functioning and sought less additional treatment

NOTE: RR = respiratory rate; PDSS = Panic Disorder Severity Scale; ASI = Anxiety Sensitivity Index; BDI = Beck Depression Inventory; STAI-T = State-Trait Anxiety Inventory, trait version; FU = follow-up; IIR = in-situ isometric relaxation; CM = cognitive modification; IR = imaginal rehearsal; CBT = cognitive-behavioral therapy; BT = breathing training; EX = in-vivo exposure; IEX = interoceptive exposure; CR = cognitive restructuring; WL = waiting list control.

taught to reattribute the cause of their panic attacks to stress-induced hyperventilation. A pacing audiotape (12 breaths per minute) was used to teach patients slow and regular breathing. Participants performed voluntary hyperventilation initially to support the therapy rationale and again at the end of treatment to test their abilities to control their symptoms. The BT produced a substantial and rapid reduction in panic attack frequency and self-reported anxiety and depression. The authors concluded that brief respiratory training is an effective treatment for panic attacks to help patients control symptoms more effectively.

Salkovskis et al. (1986) replicated and extended the treatment introduced by Clark et al. (1985) by using repeated $p\text{CO}_2$ measurements to test whether patients suffering from panic attacks had lower resting $p\text{CO}_2$ levels before treatment and whether these levels increased during treatment. Psychological outcome variables of BT showed a significant improvement compared to baseline. PCO_2 levels rose from abnormally low levels at baseline to normal levels in the course of the therapy. The authors concluded that respiratory training can restore patients' $p\text{CO}_2$ and may therefore reduce their previously heightened vulnerability to psychological stressors. Follow-up results from this and the previous two studies, after the "pure" BT phase, were not informative because exposure and other elements had been added to the treatment.

Hibbert and Chan (1989) tried to test the effectiveness of Clark et al.'s (1985) BT and its specific usefulness in panic patients who respond to a hyperventilation challenge. One group was given BT, and a control group was given an elaborate alternative intervention, which included information on stress, the fight-flight response, arousal, and the role of personality in anxiety, followed by an exploration of individual relevance of these factors to the patient's background and history using free associations. (The term *placebo* seems hardly adequate for something so extensive.) Both treatments were effective, and self-reports from diaries and questionnaires after 2 weeks revealed no significant differences between them. Because participants were given 3 weeks of exposure following both treatments, the combined effect of BT plus in vivo exposure versus placebo treatment plus in vivo exposure can be estimated. Observer ratings (Hamilton Anxiety Rating

Scale) 3 weeks after the last exposure session indicated more improvement in participants receiving BT, whereas self-reports again suggested that both groups improved equally. There was no evidence that responders to the hyperventilation test benefited more from BT than nonresponders, which the authors interpreted as evidence that BT effects were nonspecific. Follow-up was limited to 3 weeks after treatment.

Meuret et al. (2001) have described the methodology of their ongoing BT controlled study and results from 4 participants. The 4-week biofeedback therapy is aimed at voluntarily increasing self-monitored end-tidal $p\text{CO}_2$ and reducing respiratory rate and instability with breathing exercises in participants' environments. Panic attack frequency and severity, trait anxiety, anxiety sensitivity, and depression were greatly improved. Physiological data obtained by 24-hour ambulatory monitoring pretherapy and posttherapy, home training, and laboratory assessment at follow-up indicated that patients started out with low resting $p\text{CO}_2$ levels, increased those levels during therapy, and maintained them at posttherapy and/or at 2-month follow-up.

The studies above, except for Hibbert and Chan (1989), lack statistical comparison with a control group, so the extent of spontaneous remission could not be estimated. The controlled study of Hibbert and Chan suggested a greater efficacy of BT as rated (Hamilton Anxiety Rating Scale) by the therapists but not by the patients themselves.

BT COMBINED WITH OTHER INTERVENTIONS

The first controlled study of BT in panic disorder was reported by Bonn et al. (1984). Agoraphobic patients with panic who had responded with panic symptoms to a standard hyperventilation test were alternately allocated to one of two treatment groups: either two sessions of BT followed by seven weekly sessions of real-life exposure, or real-life exposure alone for 9 weeks. During therapy, patients' ratings of weekly panic attack frequency, global phobia score, agoraphobia, and somatic symptoms differed little between groups. Immediately after treatment, BT plus exposure was at least as effective as exposure alone and was superior at a 6-month follow-up in terms of

resting respiration rate, improvement in global phobia score, somatic symptoms score, and the elimination of panic attacks. A problem with this study is that the outcome measures (e.g., unspecified somatic symptom scores), although having some face validity, are not commonly used in research, and their reliability and validity are unknown. In addition, patients reporting distressing symptoms during voluntary hyperventilation (67% of the patients) apparently could have been preferentially assigned to the BT group. Patients with greater respiratory disturbances might have more difficulty in changing their breathing patterns during the relatively short 2-week BT protocol.

Franklin (1989) studied 8 patients who had agoraphobia with panic attacks to evaluate the short-term effectiveness of BT compared to “in-situ isometric relaxation” (essentially, techniques to relax quickly and effectively), cognitive modification, and a placebo treatment (“imaginal rehearsal”). Four patients were treated with four different sequences of these interventions, and 4 control patients were treated with the same sequences after a 4-week waiting period. Effects of BT were evaluated from patients’ ratings on a daily anxiety questionnaire and on behavioral avoidance measures at the beginning and completion of treatment. Methods and results of this study are poorly described. BT was reported to produce highly significant reductions in panic attack frequency and intensity, and it was the only component that produced significant improvements in the behavioral measures of agoraphobia. Relaxation produced significant reductions in frequency but not intensity of panic attacks. Cognitive modification reduced cognitive distress significantly, but it affected no other measure. Limitations of the study include its small number of subjects and possible interactions of the interventions over time, which precluded estimates of longer term outcome of BT.

Craske et al. (1997) treated patients with panic disorder and agoraphobia with group-administered cognitive restructuring and in vivo exposure; they sought to determine whether BT or interoceptive exposure added significantly more to this treatment. Both groups started treatment with three sessions of education and cognitive restructuring followed by two sessions of either BT or interoceptive exposure. Group differences at posttreatment suggested that treatments were equally effective on most of the 27 measures related to anxiety and

distress such as panic apprehension, panic fear and avoidance, agoraphobic fear and avoidance, and general distress. Significant reductions with interoceptive exposure were seen in 5 measures: panic attack frequency (only self-reported frequency at follow-up), overall severity and impairment, and agoraphobic and social fears (at the 6-month follow-up). Follow-up results have to be interpreted with caution because of the high attrition rates (28% in BT, 25% in interoceptive exposure). The authors concluded that interoceptive exposure adds more to cognitive restructuring and in vivo exposure than BT.

In patients with panic disorder with or without agoraphobia, Schmidt et al. (2000) investigated the differential effectiveness of group-administered cognitive-behavioral treatment (CBT) (education, cognitive restructuring, interoceptive exposure, and in vivo exposure) versus CBT plus BT, in comparison to a delayed-treatment control group. Their protocol was similar to that of Craske et al. (1997). Posttreatment and 12-month follow-up indicated a greater improvement in the treated versus waiting-list groups. Overall, active treatment groups were statistically similar on all outcome measures. However, patients in the CBT group showed a trend toward higher composite recovery measures for high end-state functioning and sought less additional treatment than the CBT and BT group. The authors concluded that the addition of BT was no clear benefit to the CBT package and might even have been detrimental by producing less complete recovery and a greater risk of relapse.

In summary, the four controlled studies that added BT to other therapy components offer a mixed picture of the efficacy of BT. Whereas two studies with small patient numbers showed greater efficacy of BT at posttherapy (Franklin, 1989) or at longer term assessments (Bonn et al., 1984), the two studies of Craske et al. (1997) and Schmidt et al. (2000) with somewhat larger samples did not find BT following CBT to be more effective at posttreatment or at follow-up than interoceptive exposure following CBT.

In general, comparing studies is difficult because of inconsistency in outcome instruments. Although later studies had some common outcome measures such as self-reports of panic frequency and severity or avoidance, earlier studies used instruments of unknown validity and reliability. Only in the 1990s did studies begin to employ currently

accepted instruments. Surprisingly, physiological outcome measures, such as measures of respiration, were included in only three of the nine BT studies (Bonn et al., 1984; Meuret et al., 2001; Salkovskis et al., 1986). This is a serious deficiency because BT interventions target measurable physiological processes. Furthermore, patient groups could not easily be compared across studies: Whereas some studies were restricted to patients with panic disorder or agoraphobia sensitive to voluntary hyperventilation, others drew from a larger population of patients with panic disorder or patients with agoraphobia. Only Hibbert and Chan (1989) attempted to control this source of variance.

A more basic problem in designing trials that compare different treatments is to guarantee that the treatments are as distinct as they seem and work as they are intended. It is hard to imagine an effective BT treatment that does not change cognitions about panic because alleviation of panic attacks by any means should reduce catastrophic thinking. The rationale of BT contradicts the thought that sensations accompanying panic are harbingers of catastrophic illness; BT is based on the thought that the sensations are simply the product of hyperventilation in a healthy person. By the same token, cognitive restructuring may reduce the number of panic attacks by reducing anxiety in a nonspecific way that normalizes respiration so that hyperventilation panic attacks are less likely to be triggered. Relaxation therapies might work more through changing breathing than through muscle relaxation. Establishing causality is outside the reach of almost any clinical study in psychology, but in every study, essential information as to what factors are important and unimportant in BT can be provided by well-designed self-reports and questionnaires describing cognitions and by adequate physiological measures of breathing.

RATIONALES FOR BT

The rationales offered for BT varied considerably depending on the etiological model of panic the investigator espoused; these principally included hyperventilation-based and cognitive therapy-based panic models. A hyperventilation-based model in the broadest sense

assumes that hyperventilation is primary in the development of panic disorder in that it is the ultimate source of the symptoms that are perceived as catastrophic (Ley, 1992). Therefore, the rationale offered to patients must focus on reducing of hypocapnic breathing in a wide range of situations. Some therapists assume a primary role for hyperventilation only in a subgroup of patients with panic disorder: for example, those who, when instructed to hyperventilate, recognize a marked similarity between their physical sensations and those they remember from previous panic attacks. This assumption can lead to offering BT only to those with a positive response to a hyperventilation challenge, as in the study of Bonn et al. (1984). The early uncontrolled studies of BT shared this approach (Clark et al., 1985; Rapee, 1985; Salkovskis et al., 1986). A drawback of this point of view is that not all patients with panic disorder are suitable for BT, although Bonn et al. (1984) found that almost all of their pool of patients with agoraphobia (20 of 21) met criteria for being hyperventilators and could be admitted to the study.

In contrast, a cognitive model of panic development inspired by Clark (1986) relegates treating hyperventilation to a secondary role in therapy. Cognitive therapists typically tell patients that hyperventilation, like a variety of other sources of physiological symptoms, is harmless and constitutes no threat to the individual's well-being. What is more important is the maladaptive overinterpretation of symptoms that induces the panic patients to hyperventilate, with a consequent escalation of fear. This message was given, for example, in the studies of Craske et al. (1997) and Schmidt et al. (2000). Patients received a detailed account of the physiological basis of various sensations associated with hyperventilation, and they were reassured that hyperventilation is a harmless part of a normal fight-flight response. Of course, from the standpoint of hyperventilation theories of panic, this is problematic because it could lull patients into the belief that hyperventilation is normal and need not be combated. Cognitive therapists may teach counterhyperventilation techniques as a coping skill to relieve temporarily unpleasant bodily sensations but worry that this skill can be abused as a safety aid, working against the ultimate success of a cognitive exposure-based therapy (Craske et al., 1997; Schmidt et al., 2000).

These CBT rationales are quite different from the hyperventilation-based rationale, which is to reduce dysfunctional, nonadaptive breathing in a wide range of daily situations. The goal of BT should be not only to teach patients “to learn that they do not have to fear bodily perturbations produced by hypocapnia” (Schmidt et al., 2000, p. 423) but also to eliminate, as much as possible, both acute and chronic hypocapnic breathing (Meuret et al., 2001).

In fact, the countertherapeutic or detrimental effects of BT feared by Craske et al. (1997, p. 96) and Schmidt et al. (2000) have not materialized. Schmidt et al. found no negative group effects from teaching BT, and Craske et al. found that non-BT groups did better on only a small number of measures. The other controlled studies demonstrated beneficial effects of BT at posttreatment (Franklin, 1989) or follow-up (Bonn et al., 1984; Hibbert & Chan, 1989).

There are other rationales for BT than the hyperventilation and cognitive ones. For example, from the perspective of Klein’s (1992) suffocation false alarm theory, BT might serve to reset the hypothesized suffocation alarm system. From a conditioning perspective (Bouton, Mineka, & Barlow, 2001), BT could promote interoceptive exposure to sensations important for panic, such as dyspnea and chest tightness, which may be elicited by the prescribed slow and shallow breathing. In addition, some relaxation- and meditation-oriented treatments consider slow breathing to be anxiolytic in itself, regardless of whether the person had previously been hyperventilating. Stanescu, Nemery, Veriter, and Marechal (1981) wrote that “according to practitioners hatha-yoga produces a state of well-being and quietness of the mind and develops a psychophysical equipoise” (p. 1625). Oddly, some of these techniques prescribe taking deep breaths, which may promote hyperventilation.

TECHNIQUES OF BT AND THE PHYSIOLOGY OF BREATHING

Table 2 gives an overview of the different BT techniques and protocols in the controlled studies we reviewed. We took information from method sections of published papers or, in two studies, from unpublished treatment manuals (Craske et al., 1997; Schmidt et al., 2000).

TABLE 2
Breathing Training Methods in Controlled Studies

<i>Study</i>	<i>Abdominal Breathing</i>	<i>Pacing Aid</i>	<i>Breaths per Minute</i>	<i>Duration of Exercise (minutes)</i>	<i>Frequency of Exercise</i>
Bonn, Readhead, & Timmons 1984)	Yes	Not reported	8-10	Not reported	Not reported
Hibbert & Chan (1989)	Not reported	Tape with pacing instructions	Not reported	Not reported	Not reported
Franklin (1989)	Yes	Not reported	12	Not reported	Not reported
Craske, Rowe, Lewin, & Noriega-Dimitri (1997)	Yes	Counting	Not reported	10	Twice/day
Schmidt et al. 2000)	Yes	Counting	Not reported	10	Twice/day

Most studies taught abdominal breathing as the main technique, often having participants put their hands on their abdomens and chests to facilitate learning abdominal breathing.

In general, descriptions of training methods are scanty. As pacing aids, authors report giving patients tapes with instructions (the character of which were not specified) or telling patients to pace their breathing by counting their breaths. Only two studies reported the actual target breathing rate patients were supposed to achieve. Duration and frequency of exercises were specified in only two studies. Hibbert and Chan (1989) also gave their patients overbreathing exercises in the 2nd week of training, but they did not explain the function of these exercises. These variations and uncertainties in BT techniques make it difficult to compare results.

A more basic problem is that the instructions not only may have failed to achieve normocapnia, but they actually may have promoted hypocapnia, to which panic patients are particularly sensitive. As Ley (1991, 1993) pointed out, the studies of de Ruiter et al. (1989) and Garssen et al. (1992), which found only a limited efficacy of BT for

reducing panic frequency, focused exclusively on respiratory rate, although the basics of respiratory regulation require at least attention to both rate and tidal volume. Paradoxically, instructions to slow breathing rate can reduce $p\text{CO}_2$ (de Ruiter et al., 1989), probably through an exaggerated compensatory increase in tidal volume (Ley, 1991).¹

We have observed this overcompensation in our patients (Meuret, Wilhelm, & Roth, in press). Figure 1 shows the relationship between respiratory rate and $p\text{CO}_2$ in one patient during a breathing exercise. The exercise consisted of three parts: (a) a baseline during which patients sit quietly and relaxed with their eyes closed for 2 minutes; (b) a 10-minute paced breathing phase during which patients try to increase their $p\text{CO}_2$; and (c) a 5-minute breathing phase without pacing tones during which patients maintain this breathing pattern, but with continued feedback of $p\text{CO}_2$ and respiratory rate from a capnometer. In the particular exercise illustrated, respiratory rate increased and $p\text{CO}_2$ decreased during the baseline (Figure 1a); however, pacing in the second part of the exercise did not produce the instructed increase in $p\text{CO}_2$ level (Figure 1b). The decline in $p\text{CO}_2$ was reversed only when this patient realized that she needed to decrease her depth of breathing while continuing to breathe slowly and regularly (Figure 1c).

Thus, asking patients to decrease their respiratory rate without controlling their tidal volumes may not correct aberrant breathing patterns and may even result in hyperventilation-induced hypocapnia.

Another aspect of breathing that previous studies have insufficiently addressed is regularity. Recent results from our laboratory and others suggest that persistent uneven respiration, particularly sighing, is common in patients with panic disorder even at times of low anxiety and during sleep and may lead to lowered $p\text{CO}_2$ (Abelson, Weg, Nesse, & Curtis, 2001; Stein, Millar, Larsen, & Kryger, 1995; Wilhelm, Trabert, & Roth, 2001a, 2001b). Therefore, directly targeting irregularity in breathing depth and timing could help panic patients to not hyperventilate. The hypocapnic consequences of irregular breathing are apparent from the feedback from a handheld capnometry device that we provide to our patients (Meuret et al., 2001). In addition, although not included in previous studies (Grossman et al., 1985;

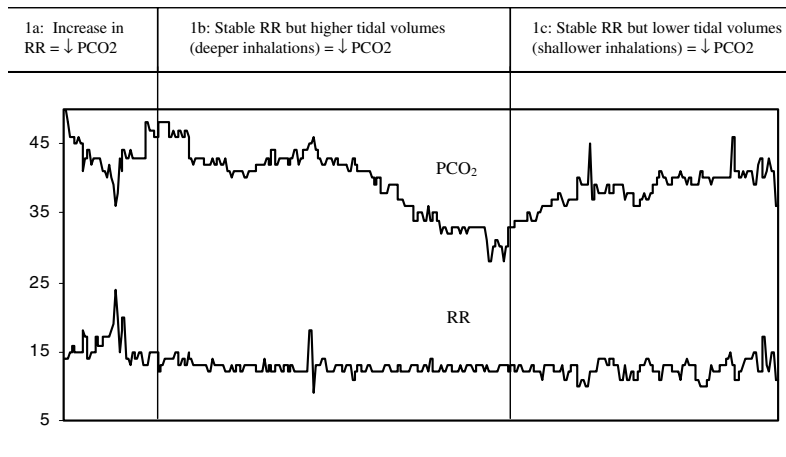


Figure 1. Example of independence between partial pressure of carbon dioxide (pCO₂) and respiratory rate (RR) during home training exercise.

Salkovskis et al., 1986; van Doorn et al., 1982), pCO₂ can be measured in the patient's own environment, thereby facilitating the generalization of learning to natural situations. Immediate biofeedback of pCO₂ alerts the patients to moments when they unconsciously increase their tidal volumes after feeling short of breath. To facilitate a regular and slow breathing pattern, patients are provided with a timed tape-recorded sequence of pacing tones. The results of each home training exercise are stored and downloaded in the electronic memory of the device for later discussion with the patient.

BT often prescribes voluntary hyperventilation exercises (Franklin, 1989; Hibbert & Chan, 1989). In such studies, the rationales and procedures are often inadequately reported. In Hibbert and Chan (1989), it is not clear why patients were given homework in overbreathing, and the extent or duration of the overbreathing actually performed was not monitored. The studies of Craske et al. (1997) and Schmidt et al. (2000) seemed to have given hyperventilation challenges to both the BT and treatment comparison groups to teach abdominal breathing for symptom control and to teach cognitive

restructuring in interoceptive exposure situations, respectively. However, the extent, duration, and frequency of hyperventilation in the different groups were not reported. Differences in these parameters between groups could have affected the reported outcomes and in general could have contributed to the inconsistent results of controlled trials of BT in panic disorder. These problems are discussed more in-depth in Meuret et al. (submitted).

BT AS A DETRIMENTAL “SAFETY AID”?

From the standpoint of at least one cognitive model of panic treatment, patients can abuse breathing techniques by using them as safety aids (Salkovskis, Clark, & Gelder, 1996). “Techniques of breathing control can be taught as ‘panic management’ techniques . . . which are likely to sustain rather than modify catastrophic cognitions” (Salkovskis et al., 1996, p. 457). Patients are able to avoid a corrective learning experience by temporarily reducing anxiety and symptoms with the techniques taught in BT, thus undermining any benefits of exposure treatment and reducing the chance for real cognitive change. However, not all cognitive therapists interpret such a use of BT as unequivocally countertherapeutic. Schmidt et al. (2000) stated that “in treatment groups, patients often recognize that this intervention is a safety aid. When this occurs, the therapist’s response is to confirm that breathing-control techniques are, indeed, safety aids” (p. 418). Similarly, Craske et al. (2000) saw a benefit in increasing a panic patient’s sense of being able to control his or her feelings. They wrote, “In fact, some evidence suggests that the primary therapeutic value of these exercises is perceived control rather than actual correction of physiological irregularities” (p. 81). These relatively negative views about IBT as safety aids are new; previous interpretations of learning theory held that an association of a BT-induced low-anxiety state with the anxiety-producing situation would lead to faster fear extinction (Wolpe & Rowan, 1988). BT should lower anxiety in anticipation of and during confrontation with the anxiety-producing situation, reduce the unpleasantness of exposure, and ultimately increase compliance and learning.

Of course, what is a safety aid and what is an essential therapeutic element for effecting permanent change is a matter of theoretical perspective. From the standpoint of a hyperventilation theory of panic, it is essential to correct underlying mechanisms responsible for the production of anxiety by targeting the habitual hypocapnic breathing pattern that also leads to symptoms such as dizziness, shortness of breath, and palpitations. From this perspective, cognitive techniques like disputing catastrophic cognitions or reassessing risks are beside the point, themselves at best safety aids giving an ultimately illusory sense of self-control. From the hyperventilation standpoint, inadequate versions of BT that fail to correct hypocapnia and interoceptive exposure that reduces anxiety without eliminating its root cause are also mere safety aids. On the other hand, from the standpoint of interoceptive exposure, correction of hypocapnia is detrimental if it temporarily dampens or eliminates the feared sensations, which the patient through habituation or other kinds of learning must grow to accept tranquilly.

pCO₂ FEEDBACK-ASSISTED BT

We have recently completed a trial of pCO₂ biofeedback-assisted BT for panic patients. We have published case studies of some initial patients (Meuret et al., 2001). The design of the trial was to assign a group of 20 patients with panic disorder to immediately begin 4 weeks of BT and to assign a second, randomly selected group of 17 to begin the same training after a 4-week delay. In accordance with a hyperventilation theory of anxiety, we assumed that correcting respiratory abnormalities such as low basal pCO₂ levels and irregularities in breathing would deprive panic of its underlying cause. The therapy protocol included an initial introductory session during which this rationale and its underlying physiology were explained to the patients in detail. Home exercises were prescribed each of the following 4 weeks. They aimed at slowing respiratory rate and increasing pCO₂ (see above for the structure of a typical exercise). Patients were taught to breathe slower and slower with the help of tape-recorded pacing tones at 13, 11, 9, and 6 breaths per minutes; the rate declines over con-

secutive weeks. The results of home exercises were reviewed at each individual weekly training session, which encouraged efforts to further increase $p\text{CO}_2$ levels by decreasing respiratory rate and tidal volume. The structured protocol and electronic data storage in the capnometer during home exercises helped enhance compliance with the training regimen. Additional 24-hour ambulatory assessments of autonomic function and respiration including expiratory $p\text{CO}_2$ were conducted before and after therapy and at comparable times in the delayed treatment group. This provided a physiological outcome measure. In addition, the initial 24-hour respiration measurements were used as an education tool, illustrating dysfunctional breathing during relevant recording periods from each individual. Initial analysis of the data (Meuret et al. 2002) confirmed that patients achieved successively lower respiratory rates and higher $p\text{CO}_2$ levels throughout training. Compared to waiting-list controls, patients' self-reports in the treatment group showed a substantial drop in panic symptomatology (as measured by the PDSS; Shear et al., 1997), anxiety (Anxiety Sensitivity Scale; Reiss, Peterson, Gursky, & McNally, 1986), and impairment in daily life (Sheehan Disability Scale; Ballenger et al., 1998). These improvements were stable (or further improvements were observed) at 2- and 12-month follow-up measurements. Effect sizes for the improvements in panic symptomatology matched or even exceeded those that have been reported for CBT interventions in panic disorder. This is remarkable considering that the traditional 13-session CBT intervention is more time-consuming. Our findings suggest that a highly structured and closely monitored BT based on a hyperventilation rationale shows considerable promise as a sufficient and enduring treatment for panic attacks.

CONCLUSION

What we know about the efficacy of BT in treating panic disorder is quite limited. Until recently, five controlled studies were available and most of them tested BT in combination with other treatment methods. While some of these studies suggest that BT is effective alone or in

combination, others suggest no substantial superiority or inferiority compared to alternative interventions. However, making a systematic comparison is difficult because of considerable variation in patient selection, study design, underlying rationales, and BT techniques. The number of ways of teaching patients with panic disorder to breathe differently was almost as large as the number of studies in our review. Studies also varied considerably in their outcome measures. They employed a variety of rating scales and questionnaires that had not been tested psychometrically in earlier studies. These limitations would make a meta-analysis unfruitful at the present.

The most logical BT is one that will reverse the specific kind of dysfunctional breathing that gives rise to panic symptoms and takes into account the basics of respiratory regulation, such as relationships between tidal volume respiratory rate and $p\text{CO}_2$. Treatment outcome measures in future studies should include changes in physiological parameters. This will make known what BT actually did, if anything. The rationale for BT in panic and the respiratory physiology underlying BT methods will probably continue to be an issue of debate. In any case, from the standpoint of hyperventilation theory, BT is neither a placebo nor a detrimental safety aid, but it is the most direct way to correct the fundamental maladaptive breathing patterns underlying panic. Our most recent findings on the efficacy of $p\text{CO}_2$ biofeedback-assisted BT support this position. Recent criticisms of BT as a treatment for panic disorder (Craske et al., 1997; Schmidt et al., 2000) are theoretically motivated and not based on empirical evidence, as we hope we have shown in this review.

NOTE

1. Instructions in the manual of Craske, Barlow, and Meadows (2000) suggest that hyperventilation is common in abdominal breathing exercises when tidal volume is not controlled:

When you first begin to count your breaths, you may become breathless or a little dizzy and begin to speed up your breathing. This should subside once you get used to the exercise. If it becomes too uncomfortable, stop for a short while and calm down, then begin again. (p. 22)

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The authors describe a new methodologically improved behavioral treatment for panic patients using respiratory biofeedback from a handheld capnometry device. The treatment rationale is based on the assumption that sustained hypocapnia resulting from hyperventilation is a key mechanism in the production and maintenance of panic. The brief 4-week biofeedback therapy is aimed at voluntarily increasing self-monitored end-tidal partial pressure of carbon dioxide (PCO₂) and reducing respiratory rate and instability through breathing exercises in patients' environment. Preliminary results from 4 patients indicate that the therapy was successful in reducing panic symptoms and other psychological characteristics associated with panic disorder. Physiological data obtained from home training, 24-hour ambulatory monitoring pretherapy and posttherapy, and laboratory assessment at follow-up indicate that patients started out with low resting PCO₂ levels, increased those levels during therapy, and maintained those levels at posttherapy and/or follow-up. Partial dissociation between PCO₂ and respiratory rate questions whether respiratory rate should be the main focus of breathing training in panic disorder.

Respiratory Biofeedback-Assisted Therapy in Panic Disorder

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Abnormalities in respiration have been postulated as a central component in anxiety disorders for several decades based on patient reports of severe respiratory distress during anxiety episodes. Shortness of breath, together with palpitations and faintness, has been found to be one of the most commonly reported symptoms of panic (McNally, Hornig, & Donnell, 1995). One hypothesis of the etiology of panic attacks specifies hyperventilation as a key mechanism in their

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production and maintenance (Bass, Lelliott, & Marks, 1989; Ley, 1985). Hyperventilation may not be limited to the attack itself but may precede and follow it, giving rise to moderate, sustained hypocapnia (Lum, 1987). According to this hypothesis, the cause of seemingly spontaneous panic attacks is often chronic or episodic hyperventilation of which the patient is generally not aware. Standardized voluntary hyperventilation produces symptoms similar or identical to panic attacks in a majority of panic patients (Bonn, Readhead, & Timmons, 1984; Clark, Salkovskis, & Chalkley, 1985; however, Griez, Zandbergen, Lousberg, & Van den Hout, 1988). Still, it remains unclear whether hyperventilation causes panic attacks or is merely an accompanying phenomenon in some panic patients (Garssen, de Ruiter, & Van Dyck, 1992). In fact, according to the suffocation false alarm theory of panic, hyperventilation is secondary to feelings of intense breathlessness. Such feelings are induced by acute rises in the partial pressure of arterial blood carbon dioxide (PCO_2), which trigger hypersensitive carbon dioxide (CO_2) sensors, resulting in acute hyperventilation. Over longer periods, chronic hyperventilation keeps PCO_2 safely below the threshold of these sensors (Klein, 1992, 1994).

The effects of hyperventilation are amplified by a positive interoceptive feedback loop according to cognitive-behavioral theories of panic. Increasing ventilation because of emotional activation causes PCO_2 to drop, resulting in an increase in pH of the blood. These changes produce a wide range of unpleasant somatic symptoms such as dizziness, breathlessness, tightness in the chest, numbness, tingling in the hands and feet, palpitations, or nausea. Panic patients often respond to these unpleasant symptoms with apprehension. This elicits further increases in ventilation, and the resulting vicious circle culminates in a panic attack (Clark, 1986). Patients often anxiously anticipate new attacks because these symptoms seem elusive and uncontrollable. As a result, the risk of new attacks increases because this anxious anticipation raises physiological activation.

Breathing training has been widely used as a component of treatment packages for panic disorder (Barlow, Craske, Cerny, & Klosko, 1989; Telch et al., 1993; Wilhelm & Margraf, 1997) and sometimes has been the sole component (Clark et al., 1985; Han, Stegen, de Valck, Clement, & Van de Woestijne, 1996; Hibbert & Chan, 1989;

Rapee, 1985; Salkovskis, Jones, & Clark, 1986). Generally, the idea behind breathing control techniques is to break the positive feedback loop (vicious circle) by reducing respiratory rate and thus increasing PCO_2 from hypocapnic to normal levels (Clark, 1986). In addition, patients learn to reinterpret their physical symptoms of hyperventilation as being a normal physiological reaction rather than life threatening. A feeling of immediate control over the symptoms should generally inhibit anxiety and panic (Wolpe & Rowan, 1988). Thus, voluntary hyperventilation has been used as an educational tool to demonstrate to patients the ideas of the vicious circle model and to reproduce feared somatic symptoms, thereby, "giving immediate relief from the longstanding feelings of helplessness" (Bonn et al., 1984). Interestingly, anxiety response to hyperventilation has not been used systematically as a diagnostic test for treatment outcome assessment, and PCO_2 , or even respiratory rate, is rarely measured during therapy.

Therapies designed to reduce hypocapnic breathing in panic disorder have usually focused on instructing patients to breathe abdominally and slowly (e.g., Clark et al., 1985; Han et al., 1996; Hibbert & Chan, 1989; Rapee, 1985; Salkovskis et al., 1986). The results of these studies were mixed. A few studies used respiratory biofeedback as a tool for reducing hypocapnia (Grossman, de Swart, & Defares, 1985; van Doorn, Folgering, & Colla, 1982) and showed efficacy of this approach. These studies were done with patients suffering from hyperventilation syndrome, a diagnosis that has a large overlap with panic disorder (Ley, 1985). The biofeedback in the study of van Doorn and colleagues (1982) consisted of about four therapist-assisted capnometry biofeedback sessions (with addition of home breathing training over 7 weeks). Patients in the study of Grossman and colleagues (1985) used a portable respiratory rate biofeedback and pacing device at home over the course of 10 weeks (in addition to seven short sessions in the clinic to adjust biofeedback settings of the device).

In addition to hypocapnia, recent results from laboratories indicate persistent respiratory pattern instability in panic patients even when they are not having panic attacks, including during sleep (Abelson, Weg, Nesse, & Curtis, 2001; Stein, Millar, Larsen, & Kryger, 1995;

Wilhelm, Gerlach, & Roth, in press; Wilhelm, Trabert, & Roth, 2001a, 2001b). We have argued (Wilhelm, Gevirtz, & Roth, 2001 [this issue]) that this instability of depth and timing of breathing from breath to breath may be a major contributor to the lowered PCO_2 levels in panic patients. These considerations would imply that teaching patients to regularize their breathing patterns may be beneficial in helping them decrease their hypocapnia.

This report describes in detail the treatment of 4 panic patients using a new methodologically improved respiratory training, utilizing respiratory biofeedback from a handheld capnometry device. The training aims at regularizing breathing patterns, reducing respiratory rates, and increasing PCO_2 in panic patients. Our study tries to answer the following questions:

1. Will this training influence panic attack severity and frequency as well as other psychological complexes associated with panic disorder?
2. Will it enable patients to increase their PCO_2 levels, decrease their respiratory rate (RR), and regularize breathing patterns?
3. Will this intervention produce long-lasting general psychological and physiological effects?

The cases presented were selected from an ongoing trial in which PCO_2 and RR are self-monitored in the patient's environment using an electronic device that reliably records pertinent information about therapy compliance and outcome. The patient's home-training efficiency, self-modification efforts, and compliance are facilitated by immediate, objective feedback of respiratory parameters. Immediate biofeedback of PCO_2 is thought to be especially beneficial because patients may feel short of breath when asked to breathe more slowly and may continue to hyperventilate by unconsciously increasing their tidal volumes. The recording allows the therapist to track patient progress without having to rely on retrospective, and possibly inaccurate or incomplete, patient self-reports, and the therapist can thereby tailor the treatment to the patient's individual needs. This approach is time and cost effective compared to paper and pencil techniques because data can be downloaded immediately, analyzed, and presented to the patient. Similar computerized assessment and therapy techniques have demonstrated the advantages of such an approach (e.g., Newman, Consoli, & Taylor, 1999; Ritz & Steptoe, 2000).

METHOD

PARTICIPANTS

In this ongoing study, participants are being recruited through paid advertisements in local newspapers. An initial phone interview screens for possible panic disorder symptoms. Qualifiers are invited for a face-to-face interview using the Structured Clinical Interview (First, Spitzer, Gibbon, & Williams, 1995) for the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.) (*DSM-IV*) (American Psychiatric Association, 1994). In addition, patients are interviewed with the Panic Disorder Severity Scale (PDSS) (Shear et al., 1997) to assess the severity and associated symptoms of panic disorder on seven dimensions (panic attack frequency and severity, anticipation, avoidance of situations and sensations, interference with work and social life). A psychologist who is experienced in structured assessments conducts the interviews. A psychiatrist conducts a second unstructured interview. Participants must be between 18 and 60 years old and meet the following additional criteria: (a) *DSM-IV* (American Psychiatric Association, 1994) Axis 1 diagnosis of panic disorder with or without agoraphobia, (b) no evidence of serious suicidal intent, (c) no evidence of current substance abuse, and (d) no evidence of schizophrenia, bipolar disorder, organic mental disorder, lung disease, epilepsy, or symptomatic heart disease. In addition, participants must be willing and able not to change the dose or kind of any previously prescribed psychoactive medication while they take part in the study.

After the initial assessment, patients are assigned to one of two conditions: an immediate treatment group or a delayed treatment control group. Patients assigned to the immediate treatment group receive five individual treatment sessions over a 4-week period. The duration of each session is approximately 80 minutes. Patients in the delayed treatment condition are reassessed after 4 weeks and then receive the same treatment. Both patient groups are reassessed following treatment and 8 weeks after treatment. The local ethics committee approved the study, for which patients provide written informed consent.

In the following, we give a brief description of the first 4 patients randomized into the immediate treatment condition with completed therapy and follow-up assessment.

Mr. A. (Patient 1) was a 44-year-old, married, unemployed man, who suffered from recurrent, unexpected and situational panic attacks. His panic attacks began 10 years ago, but in the past 7 years, his symptoms had worsened after his wife had developed multiple sclerosis. In the initial interview, he reported that even light exercising often triggered a panic attack. His main goal in therapy was to be able to exercise without panicking, because he thought that if he could do that, his other panic attacks would disappear. In the PDSS, he reported having at least one highly distressing panic attack a day. During a panic attack, he felt extremely short of breath and dizzy. An extreme preoccupation with fear and worry about panic reduced the quality of his work to a point where he was unable to continue working. Furthermore, he avoided situations such as shopping malls and social encounters. Because of fear and worry about panic, Mr. A. was severely limited in his overall functioning and lifestyle. The assessor's severity rating reflected severely disabling symptoms (PDSS total score = 27/28).

Ms. B (Patient 2) was a 40-year-old married woman, employed as a teacher. She first started having recurrent, unexpected panic attacks 10 years before coming to us, when she felt very stressed with her job. Ms. B experienced at least two highly distressing panic attacks a week. Her main symptoms included shortness of breath, heart racing, and dizziness. As a teacher, she worried about having a panic attack while in front of the class and talking to parents. She also was reluctant to wait in lines. Her main concern was that she would not get adequate, immediate help if she began to suffocate during an attack. Ms. B. labeled the interference and distress caused by her panic disorder as severe. She considered the physiological symptoms of panic attacks worse than the psychological. Her overall symptoms were assessed as severe (PDSS score = 22/28).

Mr. C (Patient 3) was a 44-year-old married man who worked as a salesman. He experienced his first panic attack 3 years before, while watching TV. On average he had two panic attacks a week, mostly unexpected but some when driving a car or at shopping malls. His

main symptoms were heart racing, chest tightness, and sweating. Mr. C. rated the attacks, as well as the anticipatory anxiety, as severely distressing and impairing. The assessor rated the overall severity of symptoms as moderate (PDSS score = 17/28).

Ms. D (Patient 4), a 40-year-old married housewife, reported her first panic symptoms after an influenza inoculation 3 years before. While driving, she suddenly felt very hot and clammy, and she perceived herself as moving while her surroundings were frozen. Six months later, she experienced a full-blown panic attack while at the hairdresser. She suddenly became very dizzy, had trouble breathing, and thought she was going to die. Since then, Ms. D. averaged more than two full-blown panic attacks a week. She felt increasingly distressed and disabled because she started avoiding anything that might trigger another attack. Her main symptoms during her attacks were lightheadedness, derealization, numbness in her arms, and hot flashes. Her overall panic symptoms were rated as severe (PDSS score = 20/28).

None of the patients took any psychotropic medications nor did they smoke while they were involved in the study.

ASSESSMENT MEASURES

A multimodal psychological and physiological assessment battery is administered to all participants at pretreatment, posttreatment, and 8-week follow-up.

Pretreatment, posttreatment, and follow-up assessment. Psychological assessments include the PDSS; the Anxiety Sensitivity Index (ASI) (Reiss, Peterson, Gursky, & McNally, 1986); the State-Trait Anxiety Inventory, trait version (STAIT-T) (Spielberger, Gorsuch, & Luchene, 1970); and the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). Physiological parameters are assessed during a 24-hour monitoring of respiratory and autonomic parameters (Wilhelm, Alpers, Meuret, & Roth, 2001) at pretreatment and posttreatment, as well as a short recording at follow-up to validate the effectiveness of breathing therapy. During this 24-hour period, patients perform five 3-minute mild hyperventilation tests and

five mild exercise (walking) tests, each followed by a 8-minute quiet sitting period, from the last 2 minutes of which PCO_2 levels and RRs are extracted. Anxiety is rated after the hyperventilation tests. Due to space constraints, we will not provide all the details of the 24-hour monitoring procedure, but interested readers can request an electronic copy by e-mailing the first author.

Assessment during therapy. Psychological changes during therapy are measured by a subset of questionnaires in the beginning of every treatment session. Physiological data from the home exercises are collected and stored by the capnometry device (see subsequent section for a description). In addition, patients fill out a breathing-training log (to rate their symptoms and emotions before and after each home exercise), a daily mood record, and a panic attack diary. Treatment compliance is calculated by the number of completed therapy sessions and completed home breathing exercises. Treatment satisfaction and credibility are measured by a modified version of the subjective rating scales by McGlynn and McDonell (1974).

BIOFEEDBACK-ASSISTED BREATHING THERAPY

The therapy contains five individual treatment sessions over the course of 4 weeks. Each session, conducted by a psychologist, lasts about 80 minutes.

Training instruments. Patients perform home-training exercises using a portable, battery-operated capnometry device (Capnocount®, Weinmann Incorporated, Germany) weighing about 320 g and measuring $65 \times 128 \times 35$ mm. The Capnocount is a side-stream capnometer that samples the exhaled gas through a nasal cannula. End-tidal PCO_2 in exhaled gases (in mm Hg) (end-tidal levels are close to arterial levels of PCO_2) (Hoffmann, Essfeld, & Stegemann, 1990) and RR (in breaths per minute, extrapolated from each breath) are analyzed and continuously displayed on the monitor. When activated, the instrument records PCO_2 and RR every 2 seconds along with the time and date of the entire measurement in its internal mem-

ory (8-hour capacity). Data can be downloaded simply with an interface module and transferred to a computer.

In addition to the visual feedback of the capnometer, patients hear over headphones a tone pattern recorded on an audio tape, guiding their breathing exertions. Rising tones indicate inspirations, falling tones indicate expirations, and silence indicates a pause between expiration and inspiration. The tone pattern is modulated to correspond to an RR of 13 breaths per minute in the 1st week and to rates of 11, 9, and 6 breaths per minute in successive following weeks. The fractional inspiratory ratio (inspiratory time per total time of a breath) was maintained at 0.4.

Self-report data prior to and at the completion of the daily breathing exercise are recorded with the diaries containing mood and panic symptoms. At the end of each day, patients rate their average level of anxiety, depression, and anticipation or worry about panic (mood record). In addition, patients rate the symptoms and emotions experienced during every panic attack immediately after its occurrence (panic attack diary).

Therapy components. The treatment includes four major components: (a) educating patients about the etiology and maintenance of panic disorder according to a hyperventilation centered rationale, (b) teaching patients techniques to control their respiration, (c) directing patients' attention to potentially aberrant respiratory patterns (awareness training), and (d) instructing patients in home breathing exercises. Treatment integrity is maintained by a structured and manualized treatment protocol that describes the specific goals and strategies for each session.

The first therapy session starts with a brief demonstration of the pretreatment 24-hour monitoring results. Special attention is paid to the raw signals of respiration (PCO_2 levels, and abdominal and thoracic breathing activity waveforms). Building on this demonstration and information, the patients are led through a series of charts explaining the rationale of the therapy, and the specific characteristics of the individual patient are addressed. The rationale is based on psychophysiological explanations of the production and maintenance of panic. The phenomenon of hyperventilation and its possible impact

on psychological and physiological parameters is discussed in detail. The role of fast, deep, and instable breathing patterns is discussed. At the end of the session, patients are provided with a therapy manual describing the planned intervention and rationale.

The first breathing technique taught is slow diaphragmatic breathing in supine and sitting positions. Once that is achieved, pacing tones are added. Then, patients learn to monitor their PCO_2 levels and RR on the capnometer while performing the paced diaphragmatic breathing. Patients learn to breathe regularly, slowly, and not too deeply, thereby maintaining or elevating their PCO_2 levels. Finally, patients are led through different breathing maneuvers (combinations of varying speed, depth, and instability of breathing pattern) using the capnometer feedback. The aim is to create an experience of the impact of changes in breathing pattern on physiological and psychological variables.

At the end of the first therapy session, patients receive detailed training in how to conduct the breathing exercises in their daily life, at home and work, and receive a detailed handout about how to maintain this. The exercises are to be performed twice a day for 17 minutes, preferably at least 6 hours apart. The exercise consists of three parts: (a) a baseline during which patients sit quietly and relaxed with their eyes closed for 2 minutes, (b) a 10-minute paced-breathing phase during which patients check their PCO_2 and RR every 30 seconds, and (c) a 5-minute breathing phase without pacing tones during which patients maintain this breathing pattern in absence of timing information but with continued PCO_2 and RR biofeedback. Timing of these phases and instructions are announced on a tape that continuously accompanies the exercises. Patients are instructed to adjust their breathing patterns to reach higher and higher PCO_2 levels.

At each weekly session (except the first), the therapist downloads the physiological data of the exercises recorded during the previous week from the capnometer and presents the data in graphs to the patients (see Figure 1). Then, the patients' psychological and physiological data are discussed, and techniques are intensified or modified according to individual needs. The application of new breathing skills during difficult situations is reviewed. The last session concentrates on maintenance of therapy gains. Principles and skills of the therapy

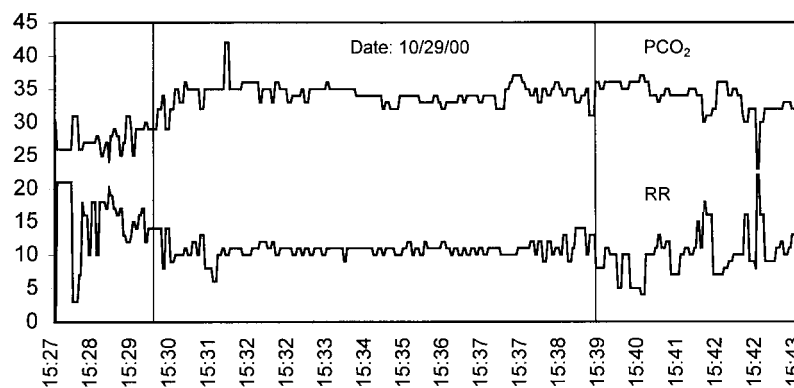


Figure 1. Printout of partial pressure of carbon dioxide (PCO_2) and respiratory rate (RR) capnometry recording for Patient 1, 2nd week, fourth breathing exercise.

are reviewed, and coping techniques for potential future stressors are discussed.

RESULTS

Compliance and credibility. All 4 patients completed the therapy including pretreatment and posttreatment 24-hour ambulatory monitoring, treatment sessions, and a follow-up assessment 8 weeks later. They showed high treatment compliance and stability (see Table 1) as measured by the number of completed therapy sessions (100%) and completed home breathing exercises with filling out the daily breathing-training log (91%, about 13 out of 14 exercises on average). This was confirmed by the date and time stamp of the capnometer recordings. Patients felt satisfied with the highly structured and monitored procedure of the breathing exercises. At follow-up, 2 of the patients reported that they had continued practicing with the exercise tapes. All 4 patients were sorry to have to return the capnometer at the end of the 4-week treatment.

All patients rated being "highly satisfied" with the therapy procedures and perceived the therapy as "very credible." The capnometer was considered extremely helpful and motivating because it gave

TABLE 1
Mean Percentage Compliance
With Home-Training Exercises by Week

	Week 1	Week 2	Week 3	Week 4	Overall Average
Home exercise (14 per week)	91	91	88	93	91
Treatment session	100	100	100	100	100

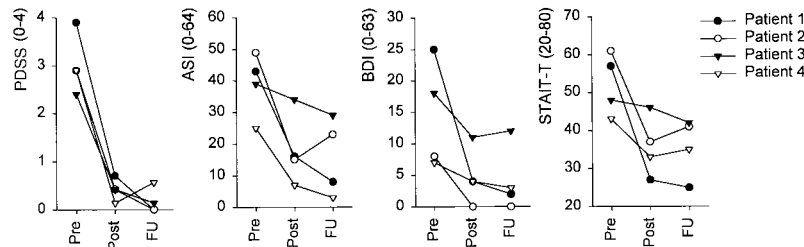


Figure 2. Individual scores for the clinician ratings (Panic Disorder Severity Scale) and questionnaires for Patients 1 to 4 during pretreatment (pre), posttreatment (post), and follow-up (FU) assessment.

immediate knowledge of the effects of changed breathing patterns and a feeling of self-control. Patients did not hesitate to perform the daily exercises in different settings, including the workplace, despite having to wear a nasal cannula while doing so.

Effects of treatment on psychological measures. Severity of panic disorder as measured by the PDSS average score (range 0 to 4) decreased substantially from pretherapy to posttherapy in all 4 patients and continued to decline in Patients 1, 2, and 3 throughout follow-up (see Figure 2). An inspection of individual ratings of the seven subscales of the PDSS showed that these improvements were achieved in all aspects of panic disorder (not shown in Figure 2). None of the 4 patients reported panic attacks at follow-up. Patient 4 experienced one limited symptom attack during the 8-week follow-up period. Also, anticipatory anxiety was strongly reduced and only mildly present in Patient 1 at postassessment. Patients 3 and 4 reported

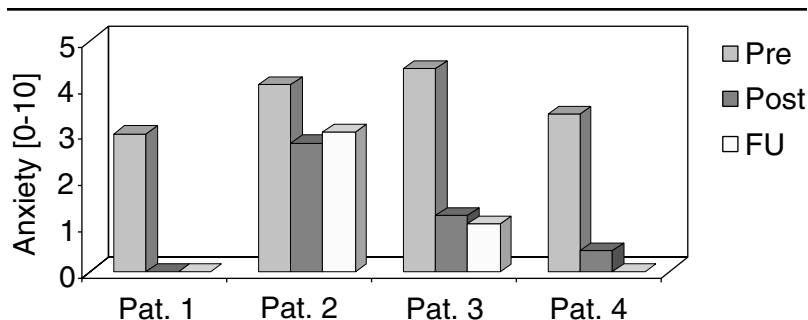


Figure 3. Individual anxiety scores during hyperventilation tests for Patients 1 to 4 during preassessment (pre), postassessment (post), and follow-up (FU) assessment.

mild worry about panic at follow-up. Mild avoidance of feared situations was reported by Patient 1 at postassessment and by Patient 4 at follow-up. According to these ratings at postassessment and follow-up assessment, all 4 patients were below the clinical threshold for diagnosis of panic disorder.

As for the self-report measures, scores on the ASI, BDI, and STAIT-T were equally reduced from pretherapy to posttherapy and follow-up for all 4 patients (see Figure 2). Clinically significant depressive symptoms were reported on the BDI by 2 patients. At the start of the treatment, Patient 1 experienced moderate symptoms ($BDI > 20$), and Patient 3 experienced mild symptoms ($BDI = 14$ to 20). At posttherapy and follow-up, depression scores were greatly reduced.

Figure 3 shows the self-ratings of anxiety during the hyperventilation tests of the ambulatory monitorings pretherapy, posttherapy, and at follow-up. Generally, anxiety decreased considerably at postassessment and declined further at follow-up.

Respiratory measures at pretreatment. Resting PCO_2 levels at pretherapy from the ambulatory assessment (see Figure 4) were overall lower than the average normal level of 39 mm Hg (Oakes, 1996), with extremely low levels (25.5 mm Hg) in Patient 3. Due to a technical failure, PCO_2 for Patient 1 could not be recorded at pretherapy assessment. RR showed clear individual differences: Although

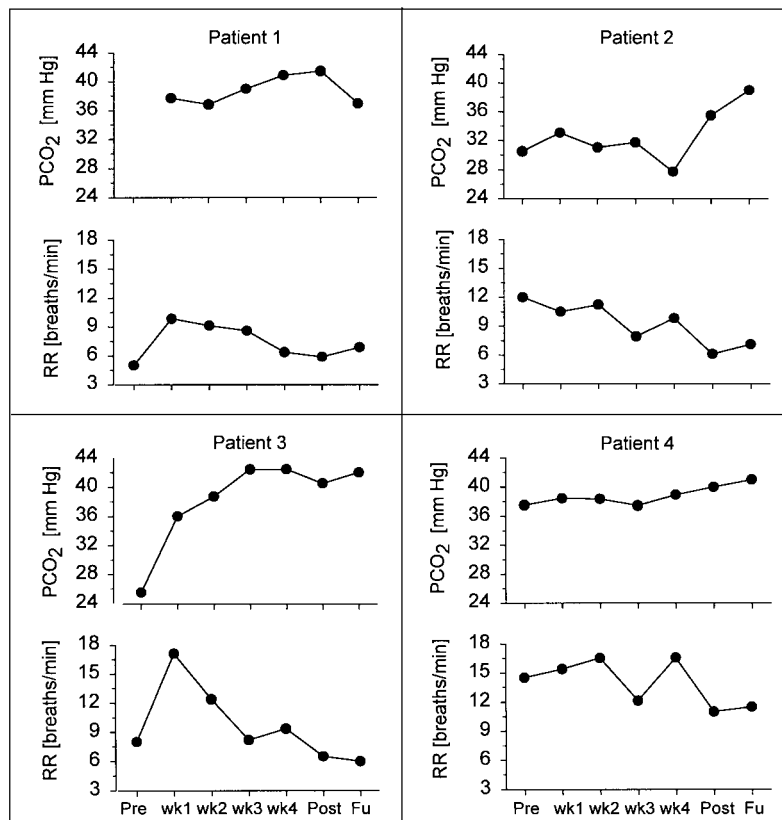


Figure 4. Individual levels of end-tidal partial pressure of carbon dioxide (PCO₂) and respiratory rate (RR) for Patients 1 to 4 from preassessment through follow-up (FU) assessment.

Patients 2 and 4 showed high rates, fairly slow rates were seen in Patients 1 and 3.

Effects of treatment on respiratory measures. Consistent with improvements in ratings for panic severity and questionnaire scores for anxiety and depression, PCO₂ during the ambulatory assessment (see Figure 4) improved from pretherapy to posttherapy. At follow-up, despite that capnometers were taken away, levels had further improved in Patients 2, 3, and 4 but had returned to pretherapy levels in

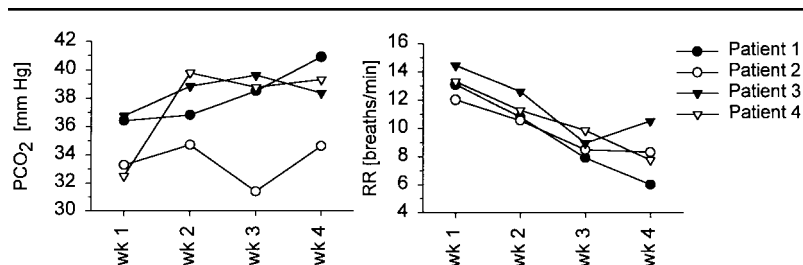


Figure 5. Individual levels of end-tidal partial pressure of carbon dioxide (PCO₂) and respiratory rate (RR) for Patients 1 to 4 during therapy, while performing paced breathing.

Patient 1. RR was clearly reduced at posttherapy and follow-up in Patients 2 and 4, was slightly reduced in Patient 3, and was slightly increased in Patient 1 at posttherapy and follow-up.

Data in Figure 4, collected during the home breathing exercises (Weeks 1 to 4), showed a more complex pattern. Each data point equals the means of the baselines before all the breathing exercises that were completed during that week. Overall, PCO₂ increased across weeks, and RR decreased. Increases in PCO₂ from pretreatment levels were small for Patient 4, varied for Patient 2, and were substantial for Patients 1 and 3. Successive decreases in RR were observed in Patients 1 and 3, while more variation was seen in Patients 2 and 4.

Figure 5 displays the means for PCO₂ and RR during the 10-minute paced-breathing exercises performed at home (see Figure 1) (Weeks 1, 2, 3, and 4 were paced at 13, 11, 9, and 6 breaths per minute, respectively). In general, patients were able to follow the tone patterns and successively lowered their RR from Week 1 to 4, with the exception of Patient 3 at Week 4. PCO₂ at Week 4 was raised above levels of Week 1 in Patients 1, 3, and 4. However, successive increments in PCO₂ were seen in only Patient 1.

Data from the breathing-training logs (ratings of symptoms and emotions before and after each exercise) were averaged for each of the 4 weeks of treatment. Overall, patients felt less anxious after completing the exercises (see Figure 6). Comparable results were found for relaxation ratings, indicating an increase in relaxation after the exercise (Figure 6). This indicates that patients felt comfortable doing the exercises and even became less anxious doing them.

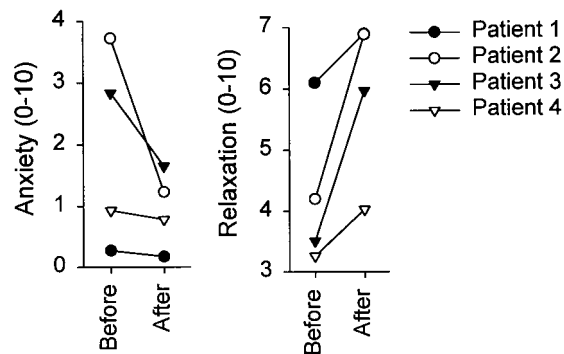


Figure 6. Individual anxiety and relaxation scores before and after breathing exercises (averaged over 4 weeks) for Patients 1 to 4.

DISCUSSION

These preliminary results from 4 patients indicate that our brief, 4-week biofeedback therapy aimed at regularizing breathing pattern, increasing PCO_2 , and reducing RR was effective in reducing panic attack frequency and severity, symptom complaints, and other psychological characteristics associated with panic disorder. Our results are consistent with findings from earlier studies using breathing training as a treatment for panic disorder. Furthermore, even without explicit elements of cognitive restructuring and exposure, improvements were obtained in trait measures of fear such as the STAIT-T and ASI. Interestingly, BDI scores also improved, suggesting that our therapy nonspecifically benefited depression.

Patients started out with moderately to severely lowered PCO_2 levels, which are consistent with observations of others, that panic patients chronically breathe in a hypocapnic range (Ley, 1988). Patients' resting PCO_2 levels increased at posttherapy and/or follow-up. Thus, our biofeedback training effectively reduced hypocapnia. Interestingly, improvement of PCO_2 during Weeks 1 to 4 of therapy was not gradual and incremental in any of our 4 patients. Although Patient 3 showed evidence of reaching a plateau at Week 3, fluctuations from week to week were observed in the other patients. In these cases, it is not clear whether 4 weeks of training were sufficient to

achieve maximum improvements. However, at posttherapy assessments, levels of PCO_2 were overall improved above pretherapy levels. Long-term improvements reaching normal levels were obtained in Patients 2, 3, and 4.

We can only speculate about the mechanisms underlying the improvements in panic symptomatology at this point. Longer term increases in PCO_2 may have led to improvement in a "physiological buffering system" (Salkovskis et al., 1986). This would reduce PCO_2 response during acute hyperventilation brought about by external (situational) or internal (bodily sensation) stressors. Reduction of breath-by-breath respiratory instability may also have mediated the improvements in PCO_2 during therapy. Respiratory regulation shows an interesting asymmetry (Wilhelm, Gevirtz, et al., 2001): A single low-tidal volume breath can cause arterial PCO_2 to rise above the normal setpoint, with CO_2 sensors stimulating a feeling of shortness of breath and strongly increasing ventilation, thus swiftly reducing PCO_2 . On the other hand, when PCO_2 falls below the normal setpoint because of a single deep breath, the resulting reduction in stimulation of CO_2 sensors only weakly decreases ventilation, so PCO_2 normalizes relatively slowly. Thus, any disturbance to the finely tuned breath-by-breath regulation of breathing (e.g., from acute emotional activation or general apprehension) is more likely to lead to a decrease than to an increase of PCO_2 . Furthermore, because of this regulatory asymmetry, sustained apprehension may prevent PCO_2 from normalizing for a long time. Because we recorded breathing patterns in detail during the ambulatory assessment using respiratory inductive plethysmography, we will be able to address this question in future reports.

In terms of psychological mechanisms, our biofeedback breathing training probably makes patients feel more in control of their bodily reactions and makes them react less fearfully to them. This is indicated by consistent reductions in scores on the ASI and by reduced anxiety in response to the hyperventilation test. It has been suggested that acquiring a sense of mastery or control also plays an important role in better coping with panic attacks (Bouton, Mineka, & Barlow, 2001).

Contrary to prior assumptions and primary focus on RR in previous breathing trainings, RR did not seem to play such a crucial role in the

improvement of our 4 patients. The PCO_2 level at preassessment was extremely low in Patient 3 despite that RR was only 8 breaths per minute, and PCO_2 rose in spite of increasing RR in the first treatment week. A partial dissociation between PCO_2 and RR was also observed in the other 3 patients at different times during the assessment. Such dissociation must be explicable by differences in tidal volumes, which were not measured during home breathing exercises. Patients can have reduced PCO_2 levels because of above normal RRs and normal or high tidal volumes or because of normal RRs and above normal tidal volumes. The lack of PCO_2 monitoring during training could explain the relatively small improvement with standard breathing training reported in several studies (de Ruiter, Rijken, Garssen, & Kraaimaat, 1989; Hibbert & Chan, 1989; Schmidt et al., 2000). Patients in these studies may have achieved normal or even below normal RRs during exercises at the cost of above normal tidal volumes so that their hypocapnic state was not corrected. In other words, asking them to decrease their RR without being sure that they did not increase their tidal volumes may not have corrected their hypocapnia. Our data suggest that one way to make sure patients perform breathing exercises as intended (i.e., to counteract hypocapnia) is by providing immediate PCO_2 feedback. Another factor limiting efficacy of breathing training may be that only a subtype of patients with respiratory abnormality (Biber & Alkin, 1999; Hegel & Ferguson, 1997; Ley, 1992) benefits from them. Respiratory assessment before therapy may help in differential diagnosis and treatment assignment. We have recently pointed out the many advantages of a multisystem assessment for clinicians working with anxious patients (Wilhelm & Roth, in press).

Perhaps, factors not specific to our breathing training, such as situational and systematic interoceptive exposure, cognitive restructuring, or spontaneous remission, were reasons for improvement. Interoceptive exposure was not a part of the therapy rationale nor were patients supported in entering feared situations, but the beneficial effects of the therapy certainly could have encouraged more self-exposure in patients' daily lives. Similarly, although cognitive restructuring was not an explicit element of our treatment approach, the explanation of our treatment rationale can be construed as a kind of restructuring (Garssen et al., 1992). However, this broadens the con-

cept of the cognitive restructuring to include any efforts at conveying information. We could try to separate and compare the informational and feedback parts of our therapy in a future study, but some explanation of why we want patients to change their breathing would be necessary to motivate them to try to do it. Finally, but least likely, the improvements in clinical state of our patients could have occurred as a result of spontaneous remission. Consistent improvements in 3 of 4 patients with respect to anxiety, avoidance behavior, and a respiratory measure (PCO_2) argue against this assumption, but only a larger sample and statistical comparison to the delayed treatment control group will be convincing. In any case, when this study is completed, we will be in a position to present more definitive results on how well and by what mechanisms a respiratory biofeedback-assisted breathing therapy of panic disorder works.

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VOLUNTARY HYPERVENTILATION IN TREATMENT OF PANIC DISORDER

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Abstract

Voluntary hyperventilation tests have been used to induce behavioral reactions similar to those of naturally occurring panic attacks. Such tests have been applied experimentally to advance the understanding of psychophysiological mechanisms in the production and maintenance of anxiety. In behavioral therapy, voluntary hyperventilation is a way of exposing patients with anxiety disorders to sensations associated with panic. It is commonly practiced as part of breathing training to help eliminate habitual breathing patterns that can lead to hypocapnia. In this article we review studies that have applied voluntary hyperventilation in breathing training, and differentiate its roles in diagnosis, education about symptoms, training of breathing strategies, and outcome measurement. We discuss methodological issues specific to these roles and procedures. Insufficient evidence for the reliability and validity of voluntary hyperventilation tests currently limit their usefulness. We give recommendations for standardization of test procedures for research and therapy.

(144/200)

Keywords: Hyperventilation; Breathing training; Respiration; Panic ; Anxiety testing

Introduction

Hyperventilation has been considered a major factor in the symptom production in panic disorder, although theoretical approaches vary as to whether hyperventilation is considered to be the necessary cause (Bonn, Readhead, & Timmons, 1984; Ley, 1985, 1992; Salkovskis, Jones, & Clark, 1986) or one of many possible causes for panic (Barlow, 2002; Papp, Klein, & Gorman, 1993). Panic patients may be overly sensitive to the decreases in CO₂ levels (Lum, 1975). Consequently, provocation of hypocapnia by voluntary hyperventilation (VH) has drawn the attention of researchers interested in panic disorder (Antony, Brown, & Barlow, 1997; Gorman, Papp, Coplan, & Martinez, 1994; Holt & Andrews, 1989; Nardi, Valenca, Nascimento, & Zin, 2001; Papp et al., 1997; Rapee, Brown, Antony, & Barlow, 1992; Spinhoven, Onstein, Sterk, & le Haen-Versteijnen, 1992; Wilhelm, Gerlach, & Roth, 2001). Therapists have devised methods of breathing training (BT) for eliminating breathing patterns leading to hypocapnia in panic patients (Bonn et al., 1984; Meuret, Wilhelm, & Roth, 2001; Salkovskis et al., 1986). Somewhat paradoxically, VH procedures have been enlisted in support of BT e.g. (Bonn et al., 1984; Craske, Rowe, Lewin, & Noriega-Dimitri, 1997). In this review we will discuss ways that VH has been used in the BT of panic disorder, and try to identify their potential advantages and disadvantages. In doing so, we ~~to~~ contribute to more careful and standardized application of hypocapnic provocations to the assessment and treatment of panic disorder.

Much of the discussion of hyperventilation tests in the literature has been in the context of investigations of patients with “hyperventilation syndrome.” Although patients diagnosed with hyperventilation syndrome and those diagnosed with panic disorder may overlap (Cowley & Roy-Byrne, 1987), we will restrict our attention to articles that have clearly identified patients as belonging to the latter, more widely accepted and better defined category.

Example of voluntary hyperventilation in the laboratory

Despite its widespread use in studies of panic disorder, little consensus exists on standards of a VH test. Patients are typically instructed to breathe faster than normal for a certain period of time but beyond this very general feature, studies vary greatly with regard to procedural parameters and outcome assessment.

Figure 1 shows the progression of a VH challenge performed in our laboratory with a panic patient (Meuret, Wilhelm, & Roth, 2002). After approximately 1 minute, the patient met our

prescribed criteria of lowering $p\text{CO}_2$ levels to 20 mmHg at a respiratory rate of 18 breaths/minute. After 3 minutes VH the patient stopped her efforts at hyperventilation, and her $p\text{CO}_2$ began to return to its initial level. Drops and spikes indicate irregularity in the breathing patterns such as sighs or pauses.

- Insert figure 1 here -

During a VH challenge, patients typically report elevated levels of anxiety accompanied by symptoms of shortness of breath, dizziness, heart racing, trembling, and tingling or numbness in the extremities. They also may report feelings of unreality or fear of losing control. These symptoms generally subside by the end of the 8-minute recovery period but in some patients, physical symptoms, anxiety, or feelings of unreality can persist for longer periods of time.

Breathing training studies using the hyperventilation test

VH challenge is frequently used in connection with BT for panic disorder. We identified nine studies (see Table 1) that used BT as a sole component or in combination with other common treatment modules (Bonn et al., 1984; Clark, Salkovskis, & Chalkley, 1985; Craske et al., 1997; Franklin, 1989; Hibbert & Chan, 1989; Meuret et al., 2001; Rapee, 1985; Salkovskis et al., 1986; Schmidt, Woolaway-Bickel, Trakowski, Santiago, Storey, Koselka, & Cook, 2000) (Table 2). BT typically taught slow and abdominal breathing, and in the studies reviewed was applied in designs where inferences about its efficacy as a separate component could be made. Treatment duration ranged from 2 to 4 weeks, with at least one therapist-guided session per week. In the study of Bonn et al. (1984) BT and in-vivo exposure were always given together, while in other studies BT was integrated into cognitive behavioral therapy (CBT) packages (Craske et al., 1997; Schmidt et al., 2000). All of these studies included VH in one form or another. Surprisingly, although the target of the BT treatment is respiration and thus a physiological one, only few studies looked at breathing pattern or gas exchange as outcome variables.

- Please insert table 1 here -

The five controlled studies that added BT to other therapy components offered a mixed picture of the therapeutic efficacy of BT. While two studies with small patient numbers showed better efficacy of BT compared to control conditions at post-treatment (Franklin, 1989) or long-term

assessments (Bonn et al., 1984), two studies (Craske et al., 1997; Schmidt et al., 2000) with somewhat larger sample sizes did not show any superiority of BT (as added component to CBT or in comparison with interoceptive exposure) at post-treatment or follow-up assessments. The study of Hibbert and Chan (1989) found a greater efficacy of BT post-treatment as measured by therapist ratings, but not by patients' self-report. In general, results from the controlled studies do not show a marked benefit of BT in panic disorder. A more complete description of these studies and conclusions about the efficacy of BT is available in Meuret, Ritz, Wilhelm, and Roth (in press). Here we will concern ourselves with technical and conceptual issues regarding the use of VH in these studies and in BT in general, and how VH might be best conducted and utilized.

Procedures for the hyperventilation test in breathing training studies

In the BT studies we reviewed, the VH instructions, verification, and assessment of outcome varied widely (see Table 2). Test duration ranged from 1 min to 3 min and target breathing rates from 18 to 60 breaths/min. The instructed breathing pattern was often described as “fast and deep breathing”, but also sometimes as “forced ventilation”, “vigorous panting” or “fast breathing with hard exhalations.” The desired pattern often was not specified. No instructions regarding volume were mentioned in a number of studies: thus if patients in these studies panted shallowly, they may not have lowered their $p\text{CO}_2$ very much. Target $p\text{CO}_2$ levels were specified only in our own study, where we required patients in a 3-minute period to quickly reach a level of 20 mmHg and maintain it. Checking for compliance of individual patients with test instructions was reported in only two studies (Bonn et al., 1984; Meuret et al., 2001). Various test outcome measures were used, although often poorly specified. In some studies the therapist inquired in a more or less structured fashion about what symptoms had occurred during hyperventilation and whether they were similar to the patient's panic symptoms. Sometimes rating scales were given,

the details of which were not always specified. Results of the VH were reported when VH was used for diagnosis (Hibbert & Chan, 1989) or outcome assessment (Craske et al., 1997), but not when used for education about breathing (Franklin, 1989) or interoceptive exposure (Schmidt et al., 2000). Physiological measurements of the extent of hypocapnia as the indicator of manipulation success were rare. Overall, consensus on technical, procedural and outcome variables of VH in BT of panic disorder was lacking, partly because of the various ~~different~~ roles the VH takes on in BT programs, but probably also because adequate instrumentation for measuring the extent of hypocapnia (capnometers) was considered too cumbersome or expensive.

Although VH is usually conducted in an individual setting, a group setting is also possible, which is economical but also has disadvantages. Visual or tactile monitoring of the respiratory parameters of group members is possible but technically difficult. The manual of Craske (1998) says that “the therapist will need to keep encouraging clients to breathe fast and especially to exhale hard” (p.32), but clients if unmonitored may not do this out of fear of the symptoms and embarrassment about panicking in front of other people. When VH is used therapeutically, it may be easier to respond to individual differences in reactions and idiosyncratic beliefs about it in an individual setting. Data from individual patients collected in a group setting cannot be treated as independent cases in the strict statistical sense, because response in one patient can influence responses in others.

How subjects are prepared for VH is an important procedural variable that varies between studies. Bonn et al. (1984), suggested that “any suggestion of effects should preferably be avoided” and offered only what they called “minimal description of possible effects (‘slight dizziness and tingling’)” to alert their patients (and healthy controls) to unexpected and unfamiliar symptoms. Extensive prior information describing all conceivable reactions as normal and harmless is likely to reduce anxiety, which is counterproductive if VH is to be used for exposure. However, certain prior information might also increase anxiety. In an earlier BT for patients diagnosed with hyperventilation syndrome Compennolle, Hoogduin, and Joele (1979) warned their patients that they might experience severe anxiety in order to increase the impact of VH provoking a panic attack, since the investigators thought that the patient would be most receptive to explanations of the mechanisms of hypocapnia and its treatment immediately after the attack. In any case, a certain amount of preparatory information is inevitable, since an

explanation of the rationale and a discussion of risks are essential for any ethical therapy procedure. The consent form required by institutional review boards for therapy in a research context is an important source of preparatory information. Some boards in trying to make clients cognizant of all conceivable risks can make a medically rather benign procedure seem fraught with dangers that make worriers worry even more.

Roles of voluntary hyperventilation in breathing training

There are several possible roles for VH in BT therapy studies: diagnosis, education about symptoms, teaching of breathing strategies, interoceptive exposure and extinction, and outcome measure. In many studies that we reviewed, more than one role was assigned to VH.

Diagnosis. A central goal for BT in panic disorder is the reduction of hypocapnic breathing, but hyperventilation may not be characteristic of all panic patients. VH has been used to identify the subgroup of patients whose attacks are associated with hyperventilation, essentially making it a diagnostic criterion. This subgroup is thought to respond to VH with discomfort, anxiety, or panic. Some investigators have restricted their treatment to patients who respond in this way (Bonn et al., 1984; Clark et al., 1986), others used the VH to identify this subgroup in order to assign it to a particular (hyperventilation-oriented) treatment module within their study (Hibbert & Chan, 1989). Bonn et al. (1984) initially demonstrated the ability of their VH test to discriminate between panic patients and healthy controls: Participants had to breathe 60 breaths/min for at least 3 minutes unless extreme physical symptoms (e.g. dizziness) were experienced. For immediate relief from symptoms during this procedure, patients were shown how to rebreathe into a bag. If the symptoms produced were recognized by patients as being similar to those experienced “in the past”, they met the diagnostic criteria for being ‘hyperventilators’. Only 33% of their patients were able to complete the 3-min VH, and 20 out of 21 met these criteria, whereas 96% of their healthy control completed the test. (For a subsequent BT study, Bonn et al. (1984b??) selected 12 additional patients, all of whom had been identified as hyperventilators). The percentage of hyperventilators identified by Bonn et al. (1984) is high compared to Hibbert & Chan (1989), who identified 13 out of 21 patients of their BT group as hyperventilators. However, their version of the VH test seemed to have been identical to that of Clark et al. (1985), who required patients to breathe fast and deep for only 2 min. The diagnosis

was given if patients scored 60% or higher on a questionnaire assessing similarity between hyperventilation and panic experience, or 50% if both situations were identical in terms of the symptom pattern albeit different in intensity.

- Please insert table 2 here -

Although using VH as a way of diagnosing the subgroup of panic patients who will respond to BT is theoretically appealing, it lacks empirical support. Such a procedure must be justified by demonstrating that patients who react to the test in a certain way will improve more in therapy than patients who react in another way. But before that is done, the investigators must decide how the test should be conducted. There is no standard test, which is a possible reason for the percentages of identified hyperventilators varying greatly between studies. The VH protocol of Bonn et al. (1984) was likely to elicit more intense and more varied panic symptoms than the protocol of Hibbert & Chan (1989) since Bonn et al. (1984) required panting at a rate over 60 breaths/min because it would “more closely resemble the typical upper-thoracic breathing of the habitual hyperventilating patient” (p. 668), while the VH test of Hibbert & Chan (1989) seemed to have required only 2 min overbreathing. A critical parameter is likely to be the actual $p\text{CO}_2$ level the patient reaches, yet only in one BT study were $p\text{CO}_2$ levels monitored and prescribed (Meuret et al., 2001) (details of the method are in Wilhelm, Alpers, Meuret, & Roth, 2001). Reliance on the most visible behavioral aspect of VH, breathing rate, is insufficient since patients can compensate a higher rate with reductions in tidal volume, thus avoiding more dramatic falls in $p\text{CO}_2$ (Salkovskis et al., 1986). When tidal volume approaches respiratory dead space, typically about 160 ml in adults, arterial $p\text{CO}_2$ can paradoxically rise even with very high respiratory rates because there is little gas exchange between the lungs and outside air. Goals for $p\text{CO}_2$ levels and how long they are to be maintained must be established or more fearful patients will avoid hypocapnia by hyperventilating less. Another aspect of VH that has not been standardized is the assessment of symptoms experienced. Typically, intensity ratings for hyperventilation were combined with some type of similarity rating between the VH experience and typical panic attacks. Two of the three studies used identical instruments for this purpose (Clark et al., 1985; Hibbert et al., 1989), but their criteria for identifying hyperventilators from it varied. Self-report criteria used by Bonn et al. (1984) were less standardized and possibly less

strict, possibly explaining the high percentage of identified hyperventilators in their pre-treatment sample.

In order to use VH for diagnosis, the $p\text{CO}_2$ level the patient reaches is unlikely to be the only parameter that needs to be taken into account: symptoms and anxiety may also depend on initial, pre-test $p\text{CO}_2$ levels. Non-hyperventilators are more likely to begin with normal $p\text{CO}_2$ levels than panic patients with underlying hyperventilation and chronically low levels, e.g., below 30 mmHg (Bass, 1985). If symptoms and anxiety depend on *change* in $p\text{CO}_2$, initially normocapnic subjects would have to change more to reach a criterion of, say, 20 mmHg than hypocapnic subjects. Thus, if change produces symptomatic response, voluntary hyperventilation to a fixed $p\text{CO}_2$ criterion might be a weaker stimulus for patients who had already hyperventilated before the test. Different baselines may distort measures of $p\text{CO}_2$ recovery from VH as well. Relative criteria, such as reductions of $p\text{CO}_2$ to a certain proportion of the initial value (e.g., Gorman et al., 1994) might be better, but data are lacking.

The amount of prior information given about the physiological background of the test and its possible effects is also likely to affect the response. Emphasis on the unpleasantness of the symptoms could amplify anxious expectancy and reactions to the test itself, while more neutral information would make the symptoms more predictable and easier to cope with. There has been little investigation of such factors, and BT studies show no consensus on this issue. Some authors gave limited descriptions of potential symptoms (Bonn et al., 1984), while others introduced VH simply as “a diagnostic test,” without specifying what symptoms might arise (Clark et al., 1985; Salkovskis et al., 1986).

Education about symptoms. Another use of VH is to teach patients how overbreathing can produce the symptoms of their naturally occurring panic attacks. This rationale is quite common in BT as seen in Table 2, but the exact educational approach differs in different studies. Franklin (1989) administered the VH test three times with varying body posture (standing, sitting, lying) and asked patients to identify the first three symptoms they experienced. Bonn et al. (1984) asked about similarities between VH symptoms and past panic symptoms, which when similar taught the patient that hyperventilation could have produced those symptoms. Hibbert & Chan (1989) used the diagnostic VH in the initial session to inform patients “that the provocation of their symptoms voluntarily by overbreathing was inconsistent with their fear that the symptoms

were a sign of physical or mental illness” (p. 233). In addition, the demonstration of hyperventilation producing symptoms was thought to be a motivator for patients to learn controlled breathing. In the second week patients, were instructed “to practice overbreathing, substituting the controlled pace” (p. 233). The overall goal of these exercises seemed to have been the achievement of greater voluntary control over breathing.

The educational aims of VH depend on the theory behind the BT. A theoretical approach emphasizing a central role for hypocapnic breathing in the etiology of panic disorder (Ley, 1985) will use VH to illustrate hypocapnic mechanisms in action and to teach patients how to counteract hypocapnia. VH presented with a rationale stressing the importance of hyperventilation in panic development can make it a powerful agent for change. Bonn et al. (1984) remarked that VH helped many patients to experience for the first time a certain degree of control over their symptoms, giving “immediate relief from longstanding feelings of helplessness that are characteristic of agoraphobic patients.” (p. xx) Since patients are often unaware of hyperventilating, they might not accept an interpretation of their symptoms as hyperventilation-produced without experiencing the dramatic effect of VH and its ability to reproduce their panic symptoms. Cognitive-behavioral theoretical approaches emphasizing catastrophic misinterpretation of bodily symptoms or that these symptoms are conditioned stimuli, use VH to teach a different lesson. Hypocapnic breathing with its resulting symptoms is described as one of several natural, harmless components of the fight-flight response. This response itself is not a panic attack or a direct cause of panic attacks: the cause of the panic attack is the meaning placed on bodily changes or conditioned fear responses to them. Therapy handouts from a cognitive-behaviorally-oriented group (Barlow, 1993) contain detailed information about the physiology and psychology of fear and anxiety, such as “the fight-flight response is associated with an increase in the speed and depth of breathing [...] the feelings produced by this increase in breathing, can include breathlessness, choking or smothering feeling, and even pains or tightness in the chest.” (p. 26) Similar materials were provided by Craske et al. (1997) as introductory information in the first and second session, and as additional information following the hyperventilation exercises in therapy. These investigators had patients hyperventilate in a group setting of three to five patients for 1-1 ½ min, after which patients sat with their eyes closed and were instructed to breathe very slowly, pausing at the end of each breath. They then discussed what they had experienced in terms of similarity of symptoms to the physical symptoms of panic

attacks. After VH cognitive-behavior therapists may ask their clients about what thoughts were elicited by overbreathing in an attempt to identify individual catastrophic cognitions and to demonstrate to the client their relationship to bodily sensations.

Teaching breathing strategies. VH can be used within the therapy setting to help patients test the effects of the new breathing patterns on the anxiety and symptoms elicited by hypocapnia. Thus, symptoms are first elicited and then overcome with the help of newly learned breathing patterns (Franklin, 1989; Hibbert & Chan, 1989). Hibbert and Chan (1989) instructed patients to “practice overbreathing, substituting the controlled pace”. The learned control over breathing was to be applied during exposure, or in general when clients were anxious. Patients were not given explicit advice about where and when to practice overbreathing. Franklin (1989) instructed patients to repeat VH at least once a day and to employ the breathing control techniques as often as required.

Interoceptive exposure and extinction. In certain studies interoceptive exposure exercises employing VH have been used with the aim of extinguishing fear of symptoms such as dizziness, shortness of breath and heart racing by repeatedly having the client induce these symptoms (Craske & Barlow, 1990; Schmidt et al., 2000). In line with the theoretical background of this approach, VH is considered only one of a number of possible exercises to elicit the feared symptoms. Other exercises are spinning the head, restricted breathing through a straw, and breath holding. Exercises are often performed in a group setting. Exercises that rank high in patients ratings of similarity to panic in terms of symptom production can be repeated many times in one session and additionally at home. Although improvement in anxiety through habituation theoretically can be automatic, therapists often introduce strategies of anxiety control to be applied immediately after anxiety has been induced by VH. These strategies may be cognitive or also involve deliberate changes in breathing, e.g, switching to abdominal breathing (Craske, 1998). Thus, in CBT the VH test is used as in BT to expose patients to an anxiety-provoking situation in order to facilitate the learning of specific control strategies, sometimes breathing strategies identical to those taught in BT. Of course, to what extent eventual improvement in any of these approaches can be attributed to cognitive changes, to emotional learning at a

subcognitive level, or to alteration in breathing patterns is a causal conundrum without any easy resolution.

Outcome measure. To our knowledge, VH has been used as an outcome measure in only two studies (Craske et al, 1997; Meuret et al., 2001). This is surprising considering the widespread use of VH in therapeutic intervention in panic disorder. Regardless of whether the basic rationale assumes hyperventilation itself or the cognitive misinterpretation of hyperventilation and other symptoms as central in the development of panic, reaction to VH seems eminently relevant as an outcome measure. The results of a test recording psychological and physiological measures before and after VH should be able to reflect some aspects of therapeutic success or failure. In the study of Craske et al. (1997), patients of both breathing training and interoceptive exposure groups performed a ‘behavioral approach test’ before and after the treatment. This test included up to one minute of overbreathing. Self-reports of anticipatory anxiety before the test and maximum anxiety were collected. Apparently results did not distinguish the groups. Few procedural details of the test were given. Meuret et al. (2001) used a VH challenge as an outcome measure during 24-hr ambulatory physiological monitoring before and after therapy. This study is still in progress, so we do not know as yet how highly reactions to VH will correlate with conventional outcome measures.

The best way to use the VH test as an outcome measure depends on whether a cognitive or hyperventilation point of view is taken. From a cognitive perspective, if patients report fewer symptoms in response to VH after having being taught about effects of overbreathing and its harmlessness, and after learning strategies for combating irrational thoughts, the therapy has been successful. Change in symptom reporting is a reasonable way to capture cognitive change. However, from a hyperventilation point of view, these educational messages might create contextual demand characteristics that distort the patients’ self-reports while leaving abnormal breathing unaltered. For hyperventilation theory, what is of key importance is that patients learn how to recover quickly from hyperventilation, which is most accurately indexed by change in pCO₂ levels. The less cognitive “education” patients receive, the more accurately their self-reports will correspond to their real progress in therapy. Thus, Meuret et al. (2001) avoided any references to the initial VH test during the BT intervention. While the idea of hyperventilation-

induced panic had been mentioned as a rationale for therapy, no explicit connection between the initial VH and that rationale was made.

Reliability and validity of VH tests

In two of its roles, that of diagnosis and of outcome measure, the psychometric properties of a VH test become relevant. A reliable diagnostic test shows test-retest reliability, although if the test is reflecting an emotion such as anxiety, which can fluctuate rapidly, the interval between test repetitions will have to be short. Its validity must be established by showing its predictive value with regard to something of clinical interest. Suppose a VH test is used to diagnose a subgroup of panic patients who are habitual hyperventilators. The reliability of such a test might be established by showing that before a treatment intervention its results are reproducible if repeated at an interval that allows time for recovery from the prior test. The validity of such a test could be established by showing that BT results in more improvement in the hyperventilating subgroup than the non-hyperventilating subgroup of panic disorder patients. A valid outcome measure should be concordant with established clinical outcome measures. When panic patients report in structured interviews or questionnaires that after treatment they have fewer panic attacks than before and they function better at work or school, VH-based outcome measures should become more normal too. However, to be clinically useful the VH test would have to say something that structured interviews or questionnaires behavior measures did not, for example, by predicting relapse.

Response to the VH includes different measures and different time points, which can be conceptualized as different test items. Measures can be divided into self-report items (e.g., reports of intensity of induced emotions such as anxiety or tension, reports of symptoms, and cognitive evaluations such as similarity to previous attacks) and physiological items (e.g., level and variability of $p\text{CO}_2$, respiration rate, depth, and tidal volume, heart rate, skin conductance). Time points can be divided into pre-VH, VH, and post-VH. How these different items are related, and whether they comprise a single factor are classical concerns of psychometric theory. In any case, the reliability and validity of individual items in the test can differ empirically, and the importance of different items may depend on one's theoretical perspective about anxiety. In general, a cognitive perspective emphasizes self-report items since they index cognitions, a hyperventilation perspective emphasizes respiratory physiological items, while a more general

psychophysiological perspective insists on both as well as autonomic measures for a complete picture of emotional response. Pre-VH physiological measures might seem to be an index of whether the testee hyperventilates habitually, but is not representative in the way 24-hour monitoring is because the fear of anxious patients is likely to change their breathing before they try to hyperventilate according to instruction. Since hypocapnia and other breathing abnormalities occur during anticipatory anxiety (Alpers, Wilhelm, & Roth, submitted), pre-measures reflect an uncertain combination of how afraid an individual is of VH and whether this anxiety is manifested in respiratory changes. Self-report measures during VH register how the testee reacts to the sensations of hyperventilation, which is central to the catastrophic cognitions theory of panic and for the concept of anxiety sensitivity. Such sensations and the reactions to them are the essence of the vicious circle that amplifies anxiety, and reduction of these reactions through continued exposure to hyperventilation (interoceptive exposure) is according to those theories a sign of therapeutic progress, although for that to be true, the reduction needs to generalize beyond the therapeutic setting. On the other hand, respiratory behavior during VH indexes only compliance with instructions rather than clinical change, since that behavior is prescribed by the test instructions. Finally, post-VH measures may represent how well the individual copes with hyperventilation once it has occurred, one of the primary goals of BT from a hyperventilation theory perspective, which regards the patient's ability to rapidly raise $p\text{CO}_2$ levels back to normal after VH and maintain normal breathing patterns signs of genuine clinical improvement. In addition, frequent or sustained hyperventilation in daily life may reduce the pH buffering capacity of the blood (REF) so that recovery is slowed. Rapid recovery is likely to be manifest in both self-report and physiological measures, but the latter are more important from the hyperventilation theory perspective because they are closer to the cause of the pathological anxiety. From an empirical perspective, if a successful therapy should normalize abnormal test results, two items are especially important for panic disorder since they repeatedly have been shown to be abnormal: self-reported anxiety during VH itself, and speed of recovery of $p\text{CO}_2$, the second being more diagnostically specific (e.g., Wilhelm et al., 2001).

A primary concern about VH as a test is its apparent lack of test-retest reliability. Self-reported symptoms and distress tend to normalize when the test is prolonged or repeated. If the levels of $p\text{CO}_2$ achieved during VH are kept constant, this normalization can also be viewed as a

growing dissociation between physiology and self-report, a development observed for several anxiogenic biological provocations. For example, van den Hout, De Jong, Zandbergen, and Merckelbach (1990) found that when healthy controls lowered their end-tidal CO₂ to 50% of its initial level for 90 min, panic symptoms peaked initially, then showed a monotonic decrease and returned to baseline levels in spite of continuation of the VH. Maddock and Mateo-Bermudez (1990) administered two consecutive VH challenges in a group of panic patients. While 50 % of the patients developed symptoms of panic following the first VH test, only 25% showed symptoms after the second test that was administered 35 minutes later. Maddock and Carter (1991) concluded that “when two anxiogenic challenges are given in rapid succession, the second one is less powerful (p. 850)”. Such habituation effects are not specific to this respiratory provocation. The subjective effects of inhaling higher than normal levels of CO₂ also diminish over time (van den Hout, van der Molen, Griez, Lousberg, & Nansen, 1987). Maddock and Carter (1991) explained the low response rate to VH in the study of Gorman, Fyer, Goetz, and Askanazi (1988) as a result of habituation across provocations: In that study a VH challenge was scheduled 15 minutes after patients had been challenged with 5% CO₂ inhalations, which could have diminished the effectiveness of VH. In another study, both habituation and sensitization effects of repeated CO₂ administration have been described for individual patients (Beck & Shipherd, 1997).

On the other hand, a clinically common interpretation of the diminution of self-reported anxiogenic effects of VH with repetition is that instead of being unreliable, self-report measures are validly reflecting a loss of fear of the symptoms of hyperventilation when patients are interoceptively exposed to it, just as specific phobics can rapidly lose their fears when confronted with their phobic object or situation. In other words, the test is accurately measuring the state of anxiety experienced during hyperventilation, and reduction of that anxiety represents real clinical improvement in panic disorder. This might have been the case ~~when~~ in a study where VH challenges were the sole treatment of patients with hyperventilation syndrome, many of whom have the symptoms as patients with panic disorder (Compernelle, et al. 1979). A large group (N=106) was seen for two initial treatment sessions, during the second of which they hyperventilated and then rebreathed into a paper bag until the symptoms subsided. They were also instructed to use this VH challenge daily to induce panic symptoms at home. The authors reported that in one third of their patients panic attacks disappeared with just two sessions and

one or two follow-up visits, while the remaining patients required additional treatment for dysfunctional family interaction. This may be an example of VH test working therapeutically in patients who have become afraid of certain somatic sensations accompanying anxiety by providing interoceptive exposure. Of course, exposure to the sensations of hyperventilation may not be enough to eliminate everyone's panic attacks, since other feared sensations may not be provoked by VH or because the effects of exposure do not generalize to other contexts. Furthermore, problems in panic disorder besides panic, such as agoraphobic avoidances, may not be overcome by interoceptive exposure alone. That could be a reason for VH test self-report results not correlating well with accepted clinical outcome measures, which would detract from the validity of a VH test as an outcome measure.

From the standpoint of hyperventilation theory, clinical severity and outcome should be more closely related to physiological measures of respiration, especially $p\text{CO}_2$, than to self-report during hyperventilation. Even one "educational" VH challenge might "give immediate relief from longstanding feelings of helplessness that are characteristic of agoraphobic patients" (Bonn et al., 1984, p. 668), but this may leave untouched habitual respiratory dysfunction triggering attacks. Since the VH test prescribes respiratory behavior during the test itself, respiration during that time reflects compliance with instruction rather than clinical change, whereas the ability of the patient to rapidly raise $p\text{CO}_2$ levels back to normal after hyperventilation and maintain normal breathing patterns is what might indicate real clinical improvement.

Our ongoing study illustrates the use of post-HV physiological measures, and how there can be inconsistencies between self-report and a physiological measure. Panic patients were assigned randomly either to receive immediate BT or to wait 4 weeks for treatment (Meuret et al., 2001). They were not told the purpose of the test nor about hyperventilation-induced panic beforehand. For the test, patients were instructed to lower and maintain an end-tidal $p\text{CO}_2$ of 20 mm Hg using an audiotape of tones to pace their breathing at a fast speed while receiving visual $p\text{CO}_2$ feedback from a capnometer (see Figure 1). Panic-related symptoms (following DSM-IV criteria) and anxiety severity were rated before the VH challenge. After the challenge, patients were given 8 minutes to recover, after which they retrospectively rated their anxiety and symptoms for the hyperventilation and recovery periods. Physiological parameters such as respiration rate and $p\text{CO}_2$ were measured continuously. This procedure was repeated several times over the day (some tests were conducted and recorded at home). This test battery was repeated after 4 weeks

for both the group that had been treated (post-treatment) and for waiting list controls. In a preliminary analysis, on-going fear of respiratory symptoms measured by the respiratory subscale of the Anxiety Sensitivity Inventory (Taylor, & Cox, 1998) were markedly reduced in the immediate BT group compared to the waiting list control after 4 weeks. The first VH of the post-assessment battery compared to the first VH pre-assessment battery showed higher $p\text{CO}_2$ and lower respiration rates during recovery in the BT group than in the waiting-list group, even after changes in baseline due to therapy were controlled for. On the other hand, self-reported anxiety and symptoms during recovery decreased equally in both groups from pre- to post-assessment in spite of differences in $p\text{CO}_2$ (Meuret et al., 2002). Thus, while the positive effects of BT in reducing fear of respiratory symptoms were reflected in a physiological outcome of the VH, that effect was not seen in self-report outcomes. There was no significant difference in anxiety and other symptom ratings in both groups during hyperventilation, with exception for “shortness of breath”. Patients in the BT group reported significantly less shortness of breath during hyperventilation compared to the waiting-list control group.

Recommendations for standardization and further research

One major problem of research involving VH in panic disorder is that no common standard of performing the test has yet emerged, which makes comparisons between studies difficult. Standardization of VH should apply to instrumentation, test procedures, and reporting of test methods and results. All factors known to influence the results of the test, particularly how often it has been repeated, need to be controlled. The extent of possible standardization will depend on the actual role of VH within the particular study. While standardization of all aspects of VH should be stringent when it is used as a test for diagnosis and outcome measurement, they may have to be more flexible for its therapeutic applications. Standards ultimately are justified by showing that they result in a reliable and valid test or an effective therapeutic procedure. As of yet, VH parameters have rarely been the subject of systematic investigation, so specific parameter recommendations remain highly tentative.

Standardization for diagnosis and outcome measurement. Any VH test worth its name needs to be standardized on physiological criteria of gas exchange indicating hypocapnic breathing, most importantly inferred arterial $p\text{CO}_2$ levels (Bass, & Gardner, 1985). Drawing on previous studies (Maddock, & Carter, 1991; Wilhelm, Gerlach, et al., 2001), a target end-tial $p\text{CO}_2$ level of 20 mmHg seems reasonable. A relative target of 50% reduction from baseline

pCO₂ is an alternative, with particular appeal when patients often start out with pCO₂ below 30 mmHg. Time held at the target level needs to be specified. Times between 2 and 6 minutes are customary. A post-hyperventilation recovery period may continue to yield information for as long as 8 minutes. Hornsveld, Garssen, and van Spiegel (1995) compared different durations and depths of VH in healthy controls. Their findings suggest a minimum test duration of 3 minutes, with end-tidal pCO₂ decreasing to at least 1.9 kPa (14 mmHg) or well below 50% of baseline in order to elicit symptoms. Although 14 mmHg has been recommended by these authors, this level may require considerable exertion for normal subjects to reach. Thus, if an absolute level rather than a percentage decrease is to be the target, 20 mm Hg is more easily attainable, and should produce symptoms of hyperventilation in most subjects.

We provide pacing tones with increasing and decreasing pitch signaling inspiration and expiration to guide the rate of breathing. We also provide feedback based on continuously displayed expiratory pCO₂ as to whether the participant should breathe deeper or shallower to reach and maintain the target level. A rate of at least 18 breaths/min is reasonable, avoiding rates above 30 breaths/min since such rates are fatiguing and limit how long the participant will continue. In addition, with very quick inspirations and expirations, tidal volume cannot be sustained at a high level and may even approach dead space, which will result in a paradoxical increase in arterial pCO₂ (hypercapnia). Even worse, a measurement of end-tidal pCO₂ will in this case indicate erroneously low pCO₂ levels because the dead space air contains a high percentage of room air with very low CO₂ concentration. Thus, instructions should include references to both a fast speed and high volume of breathing and these need to be monitored either by respiratory strain gauges or by direct observation.

The outcome measures for diagnostic VH must include self-report of anxiety and symptoms, as well as physiological measurements. Self-report instruments ideally contain a set of items that capture the dimensions of symptom and mood self-report related to VH, while also being sensitive to change. Cognitions related to the VH, such as the experience of loss of control or catastrophic thoughts (such as in the Hyperventilation Questionnaire of Rapee and Medoro (1994)), should be assessed. Measures should be taken before, during, and after the VH. The speed of recovery of respiratory parameters, most importantly pCO₂ (Gorman, et al., 1988; Maddock, & Carter, 1991) are likely to be important since pCO₂ recovery is delayed in panic disorder. Autonomic measures also may be relevant, since there is evidence that skin conductance and heart rate also show delayed recovery (Wilhelm et al., 2001). The usefulness of other temporal parameters of the VH, such as speed of drop in pCO₂, requires further study.

Other variables that need to be controlled are background messages to the participant about the rationale for the VH test, and what kind of experiences can be expected, for example whether hyperventilation can produce panic or be dangerous to the health. While the actual extent of influence of information and patients' expectation needs to be studied further, investigators should strive to keep this variable constant within one study, and report on the character of initial information given to the patient. The setting of the test may also be a variable to be controlled. In a recent comparison between a VH challenge in the laboratory and experienced panic attacks during ambulatory monitoring, we observed remarkably lower intensity in some of the reported symptoms, including anxiety (Meuret, Wilhelm, Rothkopf, & Roth, 2002) in the ambulatory setting.

Reductions in response to VH when repeated have consequences for using a VH test to compare different people for diagnostic purposes. The criteria for being identified as a member of the hyperventilator panic group, will depend on how many times the test has been repeated. If prior experience of patients with voluntary or provoked hyperventilation is not controlled for, false conclusions can be drawn. For example, in the study of Hibbert and Chan (1989) patients were given a VH test to diagnose them as hyperventilators or not. In the BT group the test was part of the first therapy session prior to any treatment while in the placebo group the test was given after the treatment was over. This design was based on the assumption that a positive response to VH might have an important therapeutic effect, positively biasing the outcome of the placebo group. Although the initial three weeks of placebo treatment focused on physiological symptoms of anxiety and the fight-flight response while avoiding mentioning hypercapnia, the subsequent three weeks were focused on graded in-vivo exposure, where multiple episodes of hyperventilation probably occurred, accompanied by some reduction in the fear that they provoked. While no group differences in the number of patients diagnosed as hyperventilators by VH were reported, it is likely that more hyperventilators would have been found in the control group if the test had been performed before these control interventions. If true hyperventilators are more likely to profit from BT training, the study could have been biased.

Reductions in response to repeated VHs have uncertain implications for using a VH test as an outcome measure. These reductions may represent a therapeutic effect, or they may be independent from overall therapeutic improvement, either because they are produced by a different mechanism or because extinction of fear occurred only in the test context and no longer

indexed fear of the sensations of hyperventilation in general. If repetition effects are independent of overall therapeutic improvement, taking repetition into account might allow their validity as an index of outcome to emerge. In any case, it is important to be able to specify how often VH has been repeated in the various treatment groups. In BT studies using interoceptive exposure as a control intervention (e.g., Craske et al., 1997), the interoceptive exposure treatment probably included many trials of VH when individual patients showed a propensity for this type of symptom elicitor. The primary type of interoceptive exposure task depends on the individual patient's sensitivity (Craske, 1998). Hyperventilation exercises may be assigned to more patients in the interoceptive exposure control groups than in the BT group causing response to this test to be reduced more in this group. It is not clear from Craske et al. (1997) whether VH was practiced in the BT group that learned slow diaphragmatic breathing. The cited treatment manual (Craske, 1998) hints at this possibility, but we do not learn whether VH occurred at a frequency and intensity equivalent to that of the interoceptive exposure group. While the study design of Schmidt et al. (2000) comparing CBT (including interoceptive exposure) with BT added to CBT apparently included hyperventilation exercises as part of the BT, we are not told the relative amount of experience with VH in the two groups.

Standardization for educational and therapeutic goals. In these settings, rigid standards for VH are rarely desirable. Patients differ in their speed of developing symptoms of hypocapnia and panic, and the therapist may be interested in eliciting a certain intensity of symptoms in an individual as the endpoint of VH provocation. VH may be stopped if the patient has reached a certain intensity of symptoms or anxiety on a standardized rating scale. It is probably desirable for the patient to try breathing at at least 18 breaths/min and at two times the usual tidal volume. When equipment for measuring physiological parameters is not available, the instructor should then take extra care that patients breathe at the required rate and simultaneously increase their tidal volume markedly. Increases in tidal volume should always be part of the test instructions in order to ascertain a sufficient level of hypocapnia.

All hyperventilation provocations during treatment sessions and as many as possible additional self-directed provocations during daily life should be documented. Reports should include duration of provocation, average breathing rate and volume or estimations of these parameters, and the level of anxiety and symptoms reached on a standardized scale. Patients

should fill in diary cards for these events. The therapist also needs to determine the level of prior information patients have about hyperventilation, and their expectations about VH. This can help therapists and researchers understand potential influences of patient expectancy on the effectiveness of VH in therapy. Patients with respiratory fears and who have had panic attacks must be warned that VH can cause distress, but too much reassurance or too complete explanation of what might happen can reduce the impact of the experience or bias it.

Although in applied therapeutic settings $p\text{CO}_2$ measurements are often perceived as uneconomical and cumbersome, hyperventilation-theory oriented therapy research should make extra efforts to include them. One reason is that reduced effects of VH procedures with repetition and dissociations between self-report and physiological measures can have implications for practice. While some authors felt that one or a few educational VH challenges brought at least partial relief for panic patients, early experienced improvement may occur before the habitual respiratory perturbations that may trigger hyperventilation-induced panic are corrected. Dissociation between experienced anxiety and physiology can also limit the use of VH for teaching breathing strategies. Reduced anxiety experience with repetition of the test may be confused with success in learning the breathing strategies needed to reverse hypocapnia. Monitoring of respiration, including $p\text{CO}_2$ levels, provides essential information to the patient and therapist about how well hypocapnic challenges are being dealt with on the physiological level.

Conclusions

Our overview of BT studies in panic disorder has uncovered a number of uncertainties about the use of VH. Most important, a common reporting standard for VH tests in diagnosis and outcome measurement is needed. Specification and recording of physiological respiratory parameters is as important as that of self-report. Conceptually, a number of different roles have been assigned to VH in BT or in control interventions for BT studies, roles that are sometimes in conflict. The use of VH as a diagnostic tool or as outcome measure is complicated by an attenuation of at least self-report responses to the test. More information is needed on the extent of this response habituation in repeated tests. Ultimate test standardization depends on establishing that when VH is conducted in a specified way, specific response measures meet basic psychometric criteria of reliability and validity. Important kinds of validity would be the ability of the test to predict

which patients will benefit from which therapy, and whether improvement from a specific therapy will be sustained at follow-up. Meanwhile, we have made some tentative suggestions about plausible parameters for VH in testing and therapy, and for assessment of responses to it.

APPENDIX

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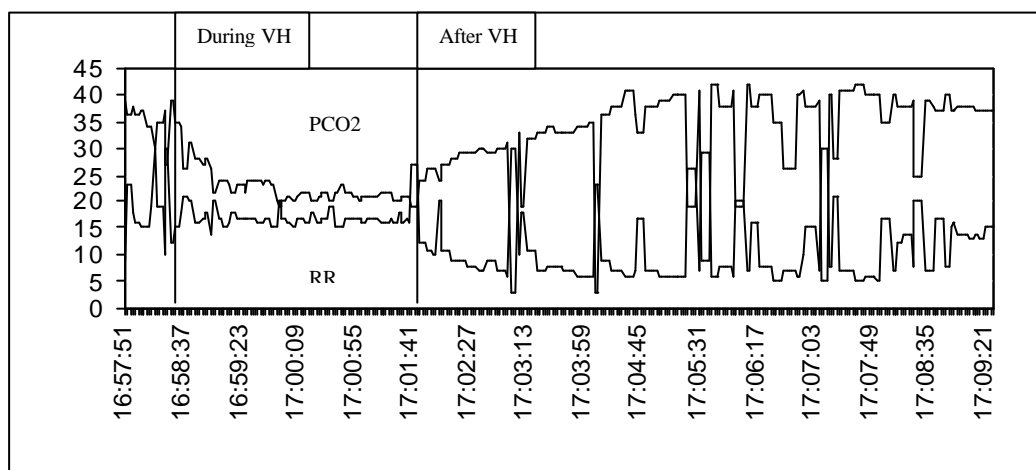
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Figures

Figure 1: Changes in pCO₂ and respiration rate during standardized VH



Tables

Table 1: Treatment breathing training studies using the hyperventilation test

Study	BT Treatment (N)	Type of BT technique	Control (N)	Type of BT outcome measures	Results for BT
Bonn et al. (1984)	2 sessions/2 weeks (plus 7 weekly sessions of in vivo exposure) (7)	Slow and diaphragmatic breathing	Exposure only (5)	Psychological and physiological	BT in combination with exposure is at least as effective as exposure alone but is superior at 6-month follow-up in terms of mean resting RR, global phobia score, somatic symptoms score and no further panic attacks.
Rapee (1985)	3 sessions/4 weeks (1)	Diaphragmatic breathing and reduction of respiratory rate and habitual sighing and yawning	-	Psychological	Decrease in panic attack frequency and severity, symptoms and anxiety.
Clark et al. (1985)	2 sessions/2 week (18)	Slow and regular breathing supported by audio-tape	-	Psychological	Reduction in panic attack frequency, self-reported anxiety and depression after 2 weeks of training.
Salkovskis et al. (1986)	4 sessions/4 weeks (9)	Slow and regular breathing supported by audio-tape (12 breaths/min)	-	Psychological and physiological	Reduction in panic attack frequency, self-reported anxiety and depression. Increase of pCO ₂ to normal levels.
Hibbert and Chan (1989)	2 sessions/2 weeks (plus 3 weeks of exposure in vivo) (21)	Paced breathing supported by audio-tape	Placebo treatment (19)	Psychological	Self-reported measures of anxiety improve equally in treatment and placebo group. At posttreatment observer but not self-report ratings indicated a greater improvement in patients receiving BT.
Franklin (1989)	1 session/4 weeks (compared to IIR, CM and IR) (4)	Slow breathing (12 breaths/min)	Delayed treatment (4)	Psychological	BT was the superior treatment in reducing panic attack frequency and severity, catastrophic cognitions, anticipatory anxiety, and behavioral measures of agoraphobia.
Craske et al. (1997)	2 sessions/2 weeks (CBT: 12 session/ 12 weeks) (18)	Slow and diaphragmatic breathing	Interoceptive exposure (20)	Psychological	Interoceptive exposure is more efficacious on certain measures than BT in combination with cognitive restructuring and in vivo exposure.
Schmidt et al. (2000)	2 sessions/2 weeks (CBT: 12 session/ 12 weeks) (21)	Diaphragmatic breathing	Delayed treatment (24)	Psychological	Active treatment groups improved statistically similarly to WL on the outcome measures. Patients in the CBT group showed a trend towards higher end-state functioning and sought less additional treatment.
Meuret et al. (2001)	5 sessions/4 weeks (4)	pCO ₂ and respiratory feedback supported training targeting slow (13, 11, 9, 6 breaths/min over course of 4 weeks), regular, diaphragmatic, shallow breathing patterns	-	Psychological and physiological	MC-PAS global scores, ASI, BDI, and STAIT-T decreased substantially from pre- to post-therapy and remained stable or declined further at follow-up.

Table 2: Techniques of hyperventilation used in breathing therapy studies

Study	Test duration	Breathing pattern	Target breathing rate	Occurrence in the therapy	Check of compliance with test instruction	Outcome criteria	Role
Rapee (1994)	1 ½ min	Not reported	25 breaths/min	Once prior to treatment	Not reported	Verbal symptoms report and judgements of similarity to past PA	- Education about symptoms
Bonn et al. (1984)	3 min	Vigorous chest panting through mouths and nose	60 breaths/min	Once prior to treatment	RR and mode of breathing was monitored	Verbal symptoms report and judgements of similarity to past PA	- Diagnosis - Education about symptoms
Clark et al. (1985)	Approx. 2 min	Fast and deep breathing through mouth	Not reported	Once prior to treatment	Not reported	Symptom rating sheet and questionnaire about similarity to past PA	- Diagnosis - Education about symptoms
Salkovskis et al. (1986)	2 min	Forced ventilation	Not reported	Repeated VHs as part of first session and home work	Not reported	Symptom rating sheet and questionnaire about similarity to past PA	- Education about symptoms
Hibbert and Chan (1989) ^a	Approx. 2 min	Fast and deep breathing through mouth	Not reported	Once in BT group in the first session, in the placebo group after the final assessment	Not reported	Symptom rating sheet and questionnaire about similarity to past PA	- Diagnosis - Education about symptoms - Training of breathing strategies
Franklin (1989)	3 times (standing, sitting, lying), up to 1 ½ min, with 30-s breaks	Not reported	18 breaths/min	Repeated VHs as part of first session and home training	Not reported	Hyperventilation questionnaire	- Education about symptoms - Training of breathing strategies
Craske et al. (1997) ^b	1- 1 ½ min	Fast breathing with hard exhalations	3x faster than normal	Repeated VH as part of breathing training and interoceptive exposure	Not reported	Discussion with therapist about symptoms produced and judgement of similarity to past PA	- Education about symptoms - Interoceptive exposure and extinction - Outcome measure
Schmidt et al. (2000) ^c	1 min	Deep and fast breathing	Not reported	Repeated VH as part of interoceptive exposure	Not reported	Symptom intensity and similarity to past PA	- Interoceptive exposure and extinction
Meuret et al. (2001)	3 min	Fast and deep	18 breaths/min	Repeated VH before and after treatment	Instructed reduction of pCO ₂ to 20 mmHg	Symptom rating and questionnaire about similarity to past PA	- Outcome measure

^a The authors cite Clark et al. (1985) for the procedure of their VH test

^b Information retrieved from therapy manual (Craske, 1998)

^c Information retrieved from therapy manual (Craske & Barlow, 1990) cited in (Telch, et al., 1993)

Effects of Capnometry-Assisted Breathing Therapy on Symptoms and Respiration in Panic Disorder

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ABSTRACT

In a randomized controlled trial, we tested the efficacy of a novel capnometry-assisted breathing therapy for reducing symptoms and regulating respiration in panic disorder (PD). Thirty-seven participants who met Diagnostic and Statistical Manual of Mental Disorders (4th ed., American Psychiatric Association, 1994) criteria for panic disorder were assigned to five sessions of breathing therapy (BT) or to a delayed-treatment control group. An assessment battery measuring the major clinical features of PD, respiration rate, and end-tidal pCO₂ was administered at baseline, posttreatment, 2-month follow-up, and 12-month follow-up. Consistent with previous studies, patients had pCO₂ levels in the hypocapnic range before they started treatment. Compared to the delayed-treatment control, the treated group improved significantly on all clinical and respiratory measures, and these improvements were maintained at follow-up. Amount of clinically significant change was comparable to that reported for cognitive-behavioral treatment. Results are discussed with respect to challenges of the utility of BT.

(words:

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Panic disorder (PD) often results in considerable emotional suffering and a reduction in quality of life. Cognitive-behavioral therapy for PD has documented success, yet we still know little about which components of cognitive-behavior packages are the active ingredients. Particularly dubious is the status of the respiratory training component, which does not fit in with the current theoretical emphasis on cognitions as the driving mechanism in panic disorder. The rationale for breathing training (BT) should come from some respiratory theory of panic, but the two available theories, the hyperventilation (Ley, 1985) and the false suffocation alarm (Klein, 1993) theories, disagree about what causes panic. Justification by the first theory is weakened by observation that hyperventilation is often absent during self-reported panic attacks (Hibbert and Pilsbury 1988; Garssen et al 1996).

As a consequence, the usefulness BT for treating panic disorder has increasingly been questioned. BT has been called a “rational placebo” (Garssen, de Ruiter, & Van Dyck, 1992) suspected of limiting improvement (Schmidt, Woolaway-Bickel, Trakowski, Santiago, Storey, Koselka, & Cook, 2000) or of being actively anti-therapeutic by acting as a false safety aid (Craske, Rowe, Lewin, & Noriega-Dimitri, 1997; Schmidt et al., 2000). Sometimes BT is conceded a role limited to patients suffering predominantly from respiratory symptoms (Schmidt et al., 2000), which might constitute a subtype of panic disorder (Biber & Alkin, 1999; Hegel & Ferguson, 1997; Stein, Millar, Larsen, & Kryger, 1995, Ley, 1992). However, in spite of such criticisms and the increasing focus on correcting irrational thinking (Barlow, 1988; Clark, 1986), BT continues to be included in multi-component treatment packages for PD. One reason may be that “patients tend to attribute a lot of change to it” (Barlow, 1997), although in Barlow’s opinion, BT is a relatively small contributor to patient improvement. Another reason may be the lack of empirical evidence for rejecting BT (Meuret, Wilhelm, Ritz, & Roth, in press-a).

BT focuses on correcting respiratory dysregulation that leads to the development or maintenance of PD. The essence of this dysregulation is hyperventilation, defined physiologically as lowered arterial pCO₂. Patients’ state anxiety is expected to covary inversely with pCO₂ level (Ley, 1985). Surprisingly, in spite of the fact that the expressed goal of BT is to correct hyperventilation, studies have almost invariably relied on self-report rather than normalization of pCO₂ for assessing outcome. Furthermore, BT usually relies on instructing patients to breathe slowly in order to correct hypocapnia, but these instructions can lead to even more hypocapnia (Meuret, Wilhelm, & Roth, in press b), probably due to an increase in depth of

breathing (tidal volume) (Ley, 1991) stimulated by feelings of suffocation. In fact, there is no convincing evidence that BT changes respiration at all, let alone in the desired direction.

Here we report results of a controlled, single-site, outcome study designed to assess the effectiveness of a novel capnometry-assisted breathing therapy (BT). Panic patients with or without agoraphobia were randomly assigned to BT or a delayed-treatment (waiting list, WL) control. After the waiting period patients received BT. Psychological and physiological data were collected before, during, and after treatment at 2-month and 12-month follow-ups. Our main hypotheses were that compared to the WL (a) capnometry-assisted BT would raise $p\text{CO}_2$ from hypocapnic to normal levels, (b) would cause a sustained reduction the frequency and severity of panic attacks and other symptoms, and that (c) physiological and psychological improvements would correlate.

METHOD

Participants

Inclusion and exclusion criteria. For inclusion in the study participants had to meet the following criteria: (a) principal DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders, 4th ed.*; American Psychiatric Association 1994) Axis I diagnosis of panic disorder with or without agoraphobia; (b) age 18 to 60; (c) no use of benzodiazepines at doses in excess of the equivalent of alprazolam 1.5 mg daily; (d) if on other psychotropic medication, on a stable dose for at least 3 months starting prior to treatment with an agreement not to change dosage at least until after the 2-month follow-up; (e) no use of drugs with pronounced sympathetic or parasympathetic effects or effects on respiration; (f) no evidence of organic mental disorder, suicide intention, schizophrenia, alcohol or drug dependence, cardiovascular disease, pulmonary disease, epilepsy, or pregnancy. Of 111 people who contacted us, 65 were excluded by the phone screening and 3 by failing to meet entrance criteria at the diagnostic interview. Of 43 clients entered into the study, 6 (4 in BT and 2 in WL) had to be excluded from analysis for the following reasons: Three patients (BT) withdrew after the initial 24-hr monitoring, one patient (BT) was diagnosed with asthma shortly after treatment, and two patients (WL) changed their medication during waiting-list period. Two patients (WL) withdrew after second 24-hr monitoring prior to the beginning of treatment because of repeated scheduling problems.

Sample characteristics. The final sample of 37 (20 BT, and 17 WL) had an average age of 41 years ($SD = 8.9$); 65% were women. A majority was Caucasian (86%), married (60%), employed (73%), and well educated (average of 17 years). The duration of the PD averaged 9 years (range 0.5-32). Twenty-seven patients (75%) had received previous treatment (medication or psychotherapy) with no or limited success. 60% suffered from panic disorder with agoraphobia, 49% had at least one secondary current Axis I diagnosis, Of these 35% had another anxiety disorder, 3 % a mood disorder, and 11% additional anxiety and mood disorder diagnoses. 32 % of the patients were taking a stable dose of psychotropic medications (16 % benzodiazepines, 11 % antidepressants, 3 % beta-blockers, and 3 % other anxiolytics). At the time of data analysis, we retrospectively classified patients as belonging to a respiratory or non-respiratory subgroup based on DSM-IV panic symptoms reported during the initial structured diagnostic interview. The respiratory group, into which 60% of our patients fell, was defined as having at least four out of the following symptoms: shortness of breath, choking, chest pain or discomfort, dizziness, or paresthesias). This method of classification was similar to that of Biggs, Stretch, & Brandon (1993).

Procedure

Participants were recruited mainly through local newspaper advertisements. A phone interview was conducted to determine diagnostic suitability. Apparently suitable candidates were then invited for a face-to-face Structured Clinical Interview for DSM-IV (SCID, First et al., 1995) and the Panic Disorder Severity Scale (PDSS, Shear, Brown, Barlow, Money, Sholomskas, Woods, Gorman, & Papp, 1997). Patients were interviewed initially by a psychologist (AEM), and then by a psychiatrist, who confirmed the DSM-IV diagnoses, evaluated the patient's medical history and medication use, and conducted a second PDSS interview. Patients were then randomly assigned to the BT or WL condition. Patients allocated to the BT condition underwent a 24-hr psychophysiological monitoring before and after therapy, while patients in the WL condition underwent 24-hr monitoring twice before therapy, four weeks apart (for detailed information see Wilhelm, Alpers, Meuret, & Roth, 2001). An abbreviated protocol of ambulatory physiological recordings was performed at posttreatment (WL only), and follow-up appointments (both groups). In addition, patients were interviewed with the PDSS and the Clinical Global Impression of Change Scale. Unlike other studies (e.g. Clark, Salkovskis, Hackmann, Wells, Ludgate, & Gelder,

1999), we did not conduct booster sessions or systematically maintain therapeutic contact after treatment had ended.

Capnometry-assisted breathing therapy. The treatment rationale was based on the assumption that sustained hypocapnea from hyperventilation is a key mechanism in the production and maintenance of panic. Hypocapnea can be a result of an increase in minute ventilation, produced by a higher respiration rate and/or tidal volumes. These higher rates or volumes could be sustained or intermittent. For example, we had observed that sighs, sporadic large increases in tidal volume, were more common in hypocapnic PD patients (Wilhelm, Trabert, & Roth, 2001a). Thus, therapy was aimed at voluntarily increasing self-monitored end-tidal $p\text{CO}_2$ and reducing respiration rate and respiratory instability by breathing exercises in the patients' natural environment. Patients underwent a four-week capnometry-assisted breathing therapy with five weekly 1-hour treatment sessions. The treatment consisted of five major components: (a) educating patients about the role of hyperventilation in the etiology and maintenance of PD, (b) directing their attention to their own potentially aberrant respiratory patterns, particularly those observed in 24-hr monitoring records, (c) having them perform different breathing maneuvers with capnometer feedback to experience how changes in breathing affect physiology and feelings, (d) teaching them ways to simultaneously control $p\text{CO}_2$ levels, respiration rate, and tidal volume, (e) and having them practice breathing exercises at home. More detailed information on the treatment protocol and case illustrations has been published elsewhere (Meuret et al., 2001; Meuret, Wilhelm, & Roth, in press-b). Other components typically found in PD treatments, such as systematic cognitive restructuring or exposure to situations and sensations other than those produced by hyperventilation, were studiously avoided in this BT.

An individual training exercise consisted of three parts: (a) a baseline period (*baseline*), during which patients sit quietly with their eyes closed for two minutes (b) a 10-minute paced breathing period (*paced*) during which patients check their $p\text{CO}_2$ and respiration rate every 30 seconds, and (c) a five-minute breathing period without pacing tones during which patients are instructed to maintain this breathing pattern and rate in absence of pacing information but with continued $p\text{CO}_2$ and respiration rate biofeedback (*transfer*). Patients were instructed to gradually adjust their breathing patterns (respiration rate, rhythm, and depths) so that they would reach or remain stable at a $p\text{CO}_2$ level around 40 mm Hg. In the first two weeks the emphasis was largely on stabilization of breathing patterns (respiration rate and rhythm), while in the last two weeks the

emphasis shifted to the more complex and initially frustrating task of normalizing pCO₂ by controlling depth of breathing in combination with lowering speed and regularizing rhythm. For the minority of patients with normal initial pCO₂ levels, treatment focused on regularity of breathing. Normal healthy adults have a mean \pm standard deviation end-tidal pCO₂ of 39 \pm 4 mm Hg (Oakes 1996). Levels higher than 45 mmHg were discouraged on the grounds that they are hard to maintain and attempts to achieve them would result in fluctuating, inconsistent breathing and unpleasant sensations. The exercises had to be performed twice a day for 17 minutes, at home or elsewhere. At the weekly sessions, the therapist downloaded the physiological capnometer data of the exercises from the previous week, and discussed the data from graphs of individual exercises. The final session concentrated on maintenance of therapy gains. Therapy principles and new skills were reviewed, and respiration-based coping techniques for potential future panic attacks were discussed.

Treatment integrity was maintained by using a structured and manualized treatment protocol (Meuret, 2000), which described the specific goals and strategies of each session. Treatment sessions, physiological recordings, and follow-up appointments were conducted by the first author, a clinical psychologist with extensive experience in the application of behavioral techniques for anxiety disorders.

Training instruments: Patients performed home-training exercises using a light (320g), handheld (65 x 128 x 35 mm), battery-operated capnometry device (Capnocount mini, Weinmann Inc.[?], Germany). The Capnocount analyzes exhaled breath pumped into the device through a transparent nasal cannula with prongs in each nostril. For this to work properly the mouth must be held closed. The instrument displays breath-by-breath end-tidal pCO₂ (mmHg) and respiration rate (breaths/min), and records them along with the time and date of the measurement in its internal memory. Such end-tidal levels are close to arterial levels of pCO₂ (Hoffmann et al, 1990). In addition to the visual feedback of the capnometer, patients were provided with a pocket-sized tape player and audiotapes to guide their paces of breathing during the exercise. A recorded voice gave instructions and announced the beginning and end of the exercises. Rising tones indicated inspirations, falling tones, expirations, and silences, the pauses between expiration and inspiration. The tone pattern were set to correspond to a respiration rate of 13 breaths per minute in the first week, and rates of 11, 8, and 6 breaths per minute in successive following weeks. At the sessions, data from individual exercises were downloaded with an interface module,

transferred to a computer, and printed out as graphs (graph 1). The Capnocount unit, tape player, and pacing tapes were returned to the therapist at the end of therapy.

Measures

An assessment battery consisting of the components listed below was administered at baseline (week 0), posttreatment (week 4), 2-month follow-up (approximately week 12), and 12-month follow-up (approximately week 52).

Panic Disorder Severity Scale (PDSS). The PDSS (Shear et al 1997) is a brief clinical rating scale based on a semi-structured interview that assesses the severity and associated symptoms of panic disorder and agoraphobia on seven dimensions (panic attack frequency and severity, anticipation, avoidance of situations and sensations, interference with work and social life) on a scale of 0 (none) to 4 (extreme). The time frame for post-treatment or corresponding waiting list assessment was the past 4 weeks, for 2-month FU assessment it was the time period since the end of treatment, and for 12 month FU assessment it was the time period since the 2-month FU. An independent interviewer who was unaware of the treatment assignment repeated the ratings. The inter-judge reliability for the PDSS composite score at the various assessment times was satisfactory ($r = .65-.90$). The composite score is the mean of the scores of the 7 items representing these 7 dimensions. According to the factor analysis of Shear et al, two factors are present, factor 1 (Item 1 and 2) and factor 2 (item 3 through 7).

The Anxiety Sensitivity Index (ASI). The 16 items in the ASI (Reiss, Peterson, Gursky, & McNally, 1986) assess the fear of the personal consequences of a variety of anxiety symptoms. Items are rated on a scale from 0 (very little) to 4 (very much).

Sheehan Disability Scale (SDS). The SDS (Sheehan, Harnett-Sheehan, & Raj, 1996) provides a self-rating of global impairment by the presenting problem. On a scale from 0 (not at all) to 10 (very severely) patients rate the degree of impairment in (a) work activities, (b) social life and leisure activities, and (c) family life and home responsibilities. Ratings on these three scales can be summed to give a composite score.

Mobility Inventory for Agoraphobia – Alone (MI-AAL). The 27-item MI (Chambless, Caputo, Jasin, Gracely, & Williams, 1985) is used to measure agoraphobic avoidance. It is sensitive to change with treatment. Patients rate the degree of current avoidance when alone to various situations on a scale from 0 (never avoid) to 4 (always avoid).

Beck Depression Inventory (BDI). The BDI (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) assesses characteristic attitudes and symptoms of depression

Clinical Global Impression of Change (CGI). The CGI (Guy, 1976) is a single Likert-type scale to assess the degree of subjective improvement compared to before treatment. Items are rated from -4 (“very much worse”), 0 (“no change”), to +4 (“very much improved”). Treatment responsiveness is defined as a rating of “much improved or “very much improved”.

Breathing training diary. Before and after each home exercise, patients were instructed to rate their symptoms (DSM-IV - PD symptoms) and emotions in weekly diaries. These diaries also included daily mood records and a panic attack log.

Physiological assessment of home exercises. Week-by-week changes in end-tidal $p\text{CO}_2$ (mmHg) and RR (breaths/min) were collected during the home exercises stored by the capnometry device to measure treatment compliance and progress. We extracted time intervals for analysis that corresponded to approximately the last 15-20% of each exercise period (last 20 s of baseline; 90 s of paced breathing; 60 s of transfer phase), because values towards the end of each measurement period were more stable and less contaminated by carry-over from previous periods. Outlier $p\text{CO}_2$ values < 15 mmHg or > 50 mmHg and RR values < 3 breath/min or > 25 breath/min were excluded to reduce the risk of including artifacts (e.g. movement, speech, coughing). The values for individual exercises were then averaged for each of the four weeks.

Physiological assessment of quiet sitting after the basal activation and voluntary hyperventilation tests. In this article we report the analysis of physiological data extracted from two standardized, supervised periods of extended quiet sitting (Wilhelm, et al., 2001). One period followed a walking test (WT) and the other a voluntary hyperventilation test (VH). These tests were conducted in the laboratory just before outside-the-laboratory ambulatory monitoring pre- and post-treatment, and at post-treatment (WL) and follow-ups without subsequent outside-the-laboratory monitoring. During the WT, patients first walk for 3 min at their normal pace and then sit quietly for 8 min. During the VH, patients breathed deeply at a rate of 1 breath every 3.3 sec for 3 minutes (equivalent to 18 breaths/min), following tones modulated sinusoidally. They received feedback from the capnometer device that displays end-tidal $p\text{CO}_2$ levels on an LCD display that guided them to increase or decrease their depth of breathing in order to quickly reach and maintain an end-expiratory $p\text{CO}_2$ level of 20 mm Hg. When the breathing tones stopped

(after 3 min), patients were instructed to resume normal breathing for the following 8 min of quiet sitting (recovery). Raw $p\text{CO}_2$ and RR data for the last 3 min of the quiet sitting periods of each test were inspected visually for artifacts (less than 10%), non-artifactual data were handscored, and means were calculated using the Variograph System (Becker Meditec[?], Germany) interactive software.

Statistical Analysis

Baseline differences between BT patients and WL on demographic and clinical variables were examined using independent t -tests for continuous variables and χ^2 -tests for categorical variables. Four major analyses were conducted: (i) Between group differences on each of the major clinical and physiological outcome measures at posttreatment were examined using one-way analysis of covariance (ANCOVA), with treatment group (BT versus WL) as the group factor and baseline levels as the covariates. (ii) One-way repeated measures ANOVAs were applied to evaluate changes in psychological measures across treatment weeks, and two-way repeated measures ANOVAs (period: baseline, paced, transfer; week: 1-4) to evaluate changes in physiological measures. Greenhouse-Geisser correction was performed for all analyses. We tested for linear trends because we expected a monotonic decrease in mood ratings, questionnaire measures of psychopathology, and RR, and a monotonic increase in $p\text{CO}_2$ across treatment weeks. (iii) To evaluate the significance of change (pretreatment through 12-month follow-up), we calculated slopes based on an analytical method suggested by Kraemer and Thiemann (1989) that was superior to ANOVAs in handling missing data due to technical problems or drop-out. No patient had to be excluded from our analysis since each had at least two data points. The method fits a curve for each subject by means of linear regression, using fractions of time corresponding to the assessment times (pretreatment, posttreatment, 2FU, 12FU). For each patient, these time points were weighted 0, 4/53, 12/53, and 1, respectively, for the regression.). 53 weeks or 13.3 months was the average measurement time for the 12-month FU. Significance of change from zero was calculated using the Wilcoxon signed-rank test. (4) Bivariate correlation analysis (Spearman, one-tailed) based on slopes (pretreatment through 12-month follow-up) was used to determine the association between physiological and psychological data.

RESULTS

Treatment credibility and compliance. Treatment credibility and satisfaction was evaluated at post-treatment (PT) and at 12-month follow-up (12FU). Self-ratings on a scale from 0-10 (“not at all” to “extremely”) were based on the following categories: (a) logicity of treatment, (b) confidence about symptom elimination, (c) confidence to recommend treatment to friends with similar problems. Patients rated the treatment extremely logical for helping people with the diagnosis of panic disorder (PT: $M=9.18$, $SD=0.98$; 12FU: $M=9.05$, $SD=1.25$). Patients felt very confident that this treatment could eliminate their panic symptoms (PT: $M=7.71$, $SD=2.27$; 12FU: $M=7.77$, $SD=2.20$) and felt highly confident in recommending the treatment to a friend (PT: $M=9.32$, $SD=0.86$; 12FU: $M=9.50$, $SD=0.86$). Ratings did not differ between time points, except for a significantly higher rating for the item “recommendation to a friend” at PT. Treatment compliance was calculated by the number of completed therapy sessions and completed home exercises (17 min of data recording and training logs). Therapy session attendance was 100%. Out of a total of 52 homework exercises over the course of four weeks, patients completed an average of 47.6 (91.3%).

Baseline characteristics. The two groups showed no significant differences in age, sex, race, marital status, employment, or education. No significant baseline differences between the groups were observed in panic disorder severity or duration, percentage of agoraphobic patients, respiratory subtype, comorbid psychiatric disorders, percent medicated, or any of the respiratory measures (respiration rate and pCO_2). The mean initial pCO_2 resting and recovery levels were, as expected, in a hypocapnic range for both groups.

Treatment outcome: treatment group versus waiting-list controls. Analyses of covariance (ANCOVAs) revealed significant effects on most psychological and respiratory measures, and a trend towards significance for resting pCO_2 (Table 1). Group by Time interactions of repeated measures ANOVAs revealed a similar pattern of significance levels. Means in Table 1 show that clinical ratings, questionnaire measures of psychopathology, and RR decreased, and pCO_2 increased in BT, whereas in WL variables showed no change or small changes in the anti-therapeutic direction.

-Insert table 1 here-

Changes across treatment weeks. At the beginning of each session, patients filled out the ASI, MI-ALL, and BDI. We used the mean values for diary ratings of anxiety, depression and worry/anticipation about panic and the means of weekly RR and pCO₂ for each phase (baseline, paced breathing, and transfer). For this and the following analyses, pre- and post- breathing training data were combined from the original BT group and from members of the WL group who continued to meet the trial inclusion criteria after the waiting period and who then received breathing training (N=15). Such combining was possible since the two groups did not differ (t-test) on any measure at pre-treatment or on slopes across treatment and follow-up. Linear trends on clinical ratings, mood ratings, and physiological variables show a steady improvement across the four weeks of training (Table 2).

RR and pCO₂ show significant improvements for all three phases of the exercises, the overall effect of weeks was $F(3,102)= 50.68$ and 5.53 , $p<.020$ and $p<.001$, $\eta^2=.70$ and $.61$, respectively. Although linear trends showed that RR decreased and pCO₂ increased significantly for each phase, these trends across weeks were steeper for paced breathing and transfer phase than for baseline (Figure 1). This was substantiated by significant interaction effects of Phase by Week for RR and pCO₂, $F(6,204)=5.76$ and 8.79 , $p=.004$ and $p<.001$, $\eta^2=.36$ and $.41$, respectively. Post-hoc tests showed that pCO₂ dropped significantly below baseline level during paced breathing and transfer in the first week (34.7 mmHg/34.5 mmHg). It then reached the highest levels (around 38 mmHg) for all three phases during the week 4. Patients were successful in following the pacing tones throughout week 3 (13, 12, and 9 cycles/min), yet they were not able to maintain the required 6 cycles/min in week 4. Values for both RR and pCO₂ during transfer improved similarly to paced breathing, a sign that patients were able to achieve and maintain a sense of volume, speed, and rhythm of their breathing patterns without direct feedback.

-Insert Table 2 and Figure 1 here-

Overall outcome across posttreatment and follow-up assessments. Table 3 shows the results of slopes (pretreatment through 12-month follow-up) on clinical and physiological outcome measures. The data is based on available data from pretreatment, posttreatment, 2-month follow-

up, and 12-month follow up. Since attrition was overall very low (dropout during treatment: N=0; dropout rate at 2-month follow-up: N=2 (2.8%); dropout rate at 12-month follow-up: N=4 (12.1%)), slopes were based (except for two patients) on at least 3 time points. Attrition was largely related to inability to contact participants who had moved.

Highly significant rates of improvement were reached on all clinical measures, and significant or marginally significant rates on respiratory measures. According to the Wilcoxon signed-rank test, patients classified, as “respiratory subtype” did not benefit more from therapy than patients who reported few or no respiratory symptoms before treatment. Furthermore, initial levels of baseline pCO₂ or respiration rate were unrelated to this classification. However, levels of pCO₂ following voluntary hyperventilation were significantly lower in the respiratory subgroup.

-Insert table 3 here-

Clinical significance of outcome. Four dimensions - panic attack frequency (PA), avoidance and disability (PDSS_AS), and clinical global impression of change (CGI) - were used to estimate response or clinical significant change to treatment. We followed the recommendations for assessment intervals of Shear, Clark, & Feske (1989) who suggest waiting at least four weeks after treatment to measure the level of *stable improvement* and at least 6 months to consider a patient in *remission*. Our follow-up assessments made at 2 months and 12 months after the end of treatment fit these recommendations. In addition, we compared BT and WL immediately after therapy or after the equivalent waiting period, respectively. We determined clinical significance similarly to Shear et al. (1989), but adding the PA as an additional dimension. To avoid overlapping criteria, only the second factor of the PDSS (item 3 through 7 – representing avoidance and interference) was used.

We also applied more stringent criteria to define response and remission. To qualify as a treatment responder, the individual patient’s PDSS_AS score had to be at least 50% below his or her baseline level, the CGI rating had to be at least “much improved”, and no panic attacks could have been experienced in the last 2 months. For remission on the PDSS_AS score had to be ≤ 2 , with all individual items ≤ 1 , for remission on the CGI, the rating had to be at least “much improved”, and for remission in panic attacks, no panic attacks could have been experienced in

the last 12 months. In addition, we computed a conjoint criterion for remission, which required remission on all three measures.

An additional calculation of clinical significance followed the psychometrically stringent criteria suggested by Jacobson, Roberts, Berns, & McClinchey (1990): Patients were defined as reliably improved at posttreatment or 2-month follow-up only if the individual improvement on the PDSS_AS exceeded the reliable change index (RC) of 1.96. Furthermore, patients met the criteria for clinical significant change on the PDSS_AS at 12-month follow-up only if they showed a reliable improvement (RC larger than 1.96) *and* fell into range of normal functioning (defined as 2SD beyond the pretreatment mean [PDSS score < 0.73]). Finally, a composite score was calculated, whereby a patient was defined as recovered only if he or she met the criteria for clinical significant change or cut-off scores on all measures. Results are presented in Table 4.

-Insert table 4 here-

Depending on the criterion, response or improvement on the PDSS (avoidance and interference) was 80% at posttreatment for patients, and 6% to 12% for waiting-list controls. 40% of the patients experienced zero panic attacks at posttreatment compared to 6% in the WL. Chi-square analysis of individuals meeting either criteria (response or improvement) showed significant superiority of BT over WL on PDSS_AS and PA. At 2-month follow-up, 54% qualified as treatment responders on all four dimensions and 35% as reliably improved. At 12-month follow-up, 64% of the patients reached the conjoint criteria for remission on all four dimensions, but only 50% when the strict criteria of Jacobson et al. were applied.

Relationship between changes in clinical and respiratory measures. We correlated the slopes individual linear regressions for selected panic and anxiety parameters (Table 5) and found significant or marginally significant correlations between recovery $p\text{CO}_2$ and respiration rate after hyperventilation, resting respiration rate, panic severity, anxiety sensitivity, and overall disability ($r=.30 - .50$). Patients who showed an overall higher level of $p\text{CO}_2$ or respiration rate recovery after hyperventilation also showed greater level of improvement in psychological measures.

-Insert table 5 here-

DISCUSSION

This study evaluated the effectiveness of a brief capnometry-assisted breathing therapy in treating panic disorder. At posttreatment the treated group but not the waiting-list group was improved significantly in panic disorder severity, agoraphobic avoidance, anxiety sensitivity, disability, and respiratory measures. Psychological and physiological measures remained improved or improved further at 2-month and 12-month reassessments. This is consistent with other studies that used computers or special devices and found that patients could maintain improvement after these technological aids were withdrawn (e.g., Newmann et al. 1997). Clinical significance at posttreatment showed superiority of the treated over the untreated group. At our 12-month follow-up, 61% of patients reported high end-state functioning. They rated our therapy as being logical and effective in treating panic disorder, an appraisal that perhaps explains their high compliance in session attendance and completion of homework exercises. There were no dropouts during treatment and very few during follow-up. We found no support for the assumption that BT is particularly beneficial for patients belonging to a respiratory subtype (e.g. Schmidt et al. 2001), although this subtype had significantly lower initial levels of pCO_2 (an average level below 30 mmHg) after voluntary hyperventilation. Perhaps greater or more sustained hypocapnia as exemplified by delayed recovery from hyperventilation (Wilhelm, Gerlach, & Roth, 2001) results in increased perception of respiratory sensations during panic attacks.

A change in the respiratory response to a provocation test after treatment suggests that patients had learned a new way to cope with anxiety. Improvement in respiratory measures was correlated with psychological improvement. Before treatment patients' pCO_2 level remained in a hypocapnic range after the 8 min recovery period, but at posttreatment pCO_2 increased into the normocapnic range after 8 min and remained stable 12 months later. More normal levels of recovery pCO_2 and respiration rate were associated with lower levels of panic severity and disability. Correlations of pCO_2 and RR after VH between the posttreatment, 2-month, and 12-month follow-up time points, indicated that patients had developed a stable respiratory compensation mechanism for hyperventilation. In the WL list, RR but not pCO_2 responses were stable. These results could be interpreted as supporting the therapy's rationale that hypocapnia

causes and maintains anxiety, and that patients can learn skills that allows them to maintain normocapnia when threatened with hypocapnia.

However, the direction of causality might be the opposite, with anxiety causing hypocapnia and breathing training alleviating anxiety by non-respiratory therapeutic mechanisms. Our breathing training could have helped by decreasing catastrophic thinking, giving patients a sense of control, encouraging interoceptive exposure and exposure to agoraphobic situations, and by providing an anxiety-reducing distraction (Craske et al., 1997; Schmidt et al., 2001). Counter to catastrophic thinking, the hyperventilation rationale delivered the message that the bodily symptoms of panic attacks are not manifestations of a health-threatening disease, but a normal part of anxiety. These symptoms have a known, benign physiological cause, which can be subjected to voluntary control. Interoceptive exposure was a consequence of the paced breathing exercises and voluntary hyperventilation tests, which trigger uncomfortable respiratory sensations similar to those previously experienced during panic attacks. Both decreasing pCO₂ with hyperventilation and increasing it in an attempt to normalize CO₂ can result in dyspnea. In addition, breathing training's nonspecific direction of patients' attention to their respiration should have facilitated exposure.

At the 12-month follow-up, patients were asked to write down what *they* considered as important for their improvement. A number of patients stated understanding and changing the symptoms of hypocapnea was the most crucial element of success. Before treatment they had felt at mercy of their own sensations, but they now felt more in control of uncomfortable physical symptoms. However, as one client stated, to achieve this level of mastery it was important to get numeric feedback from the Capnocount: "The treatment helped me understand the physical processes in my body when having anxiety/panic...to actually see a number that quantified things and to gradually learn to control my breathing allowed me to feel I could do something about my panic attacks...". As a result, patients may have been more inclined to enter agoraphobic situations. One patient said: "...the training demystified panic for me and now I feel in complete control even when I feel panicky...I know exactly why it's happening physiologically, so I am able to work though it, especially in situations which I avoided before...". When asked about their current coping mechanisms during anxious states, patients stated that they would close their mouths and start breathing through their noses shallowly and slowly for a couple of seconds until symptoms had passed. The rationale of our breathing therapy

fit well cognitively with the somatic concerns of panic patients. It not only told them *how* their physical symptoms are produced, but also that they *can* be changed and *how* to change them. If patients succeed in changing them, cognitive restructuring of their meaning becomes irrelevant.

Traditional breathing exercises, which do not monitor $p\text{CO}_2$, are in danger of producing more symptoms rather than reducing them. Traditional breathing instructions (e.g. “take deep breaths”, “breathe slow and regular”) may well intensify physical symptoms during exposure rather than reducing them (Meuret et al., 2003). This may explain why interventions did not lead to better outcomes when BT was added to the CBT package (e.g. Schmidt et al., 2001). Patients might have experienced more intense symptoms when following traditional breathing instructions, which theoretically might have intensified interoceptive exposure, but they would have failed to learn effective antihyperventilation techniques that are the basic rationale for BT.

Capnometer feedback is critically important if hyperventilation control is the goal. PCO_2 feedback also had the advantage of enforcing the reassuring message that it is actually a lack of CO_2 rather than a more dangerous lack of oxygen causing dyspnea.

Breathing training with capnometer feedback did not reach its goals instantly. Effects were different within exercises and across therapy. In the first week, when breathing was paced at a constant 13 breaths/min, $p\text{CO}_2$ typically *fell* from the beginning (baseline) to the end of the exercise (transfer). However, from week three on with 9 or 6 breaths/min, patients achieved small increases in $p\text{CO}_2$ from the beginning to the end of the exercise (Table 2). These generally small short-term increases in $p\text{CO}_2$ during the exercises contrasted with more substantial increases in $p\text{CO}_2$ over the course of therapy (Meuret et al., 2003).

Our device stores physiological data with a date and time stamp, which can be used to monitor homework. We interpret the high degree of homework compliance and non-existent drop-out during treatment as a sign that patients were intrigued by the two-fold feedback they received, namely, the direct capnometer feedback during their homework exercise and therapist feedback during treatment sessions based on capnometer data. However, like other therapeutic devices such as palm-top computers or virtual reality products to treat anxiety patients (e.g. Newmann et al., 1997; Maltby, Kirsch, Mayers, & Allen, 2002) capnometry has a cost. The Capnocount mini[®], designed as a portable emergency device, cost about \$2,500 USD. Undoubtedly as technology advances and use increases, prices will go down. Ambulatory

capnometry devices have recently been recommended by the American Heart Association to allow paramedics to verify endotracheal intubations (Cummins & Hazinski, 2000).

In summary, our results show that capnometry-assisted breathing therapy can be an efficient intervention to treat panic disorder. Capnometer feedback is the most direct and convincing way to correct fundamental maladaptive breathing patterns associated with hyperventilation. Traditional breathing training may actually increase hyperventilation because advice to slow breathing leads to increased shortness of breath and a covert increase in the depth of breathing, compensating or overcompensating for the decrease in respiration rate. Future studies of breathing training need to include pCO₂ measurements if its goal is to correct hyperventilation, since only then will we know if the goal has been attained. Other contrast groups and respiratory manipulations will be needed to untangle the several interacting factors possibly contributing to the success of breathing training.

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Table 1

Means and standard deviations of pre- and post-treatment values, pre- and post-waiting-list values, and significance of ANCOVA group effect

Measures	BT (N=20)		WL (N=17)		BT vs. WL
	Pre-TX	Post-TX	Pre-WL	Post-WL	<i>p</i>
PDSS (0-4)	2.14 (0.65)	0.69 (0.45)	1.98 (0.87)	1.95 (0.67)	0.000
SDS (0-10) ^a	2.47 (2.45)	0.73 (0.92)	3.20 (2.25)	2.77 (2.17)	0.000
ASI (0-4) ^a	1.86 (0.83)	0.92 (0.64)	1.86 (0.86)	1.58 (0.72)	0.000
MI-AAL(1-5) ^a	1.86 (0.60)	1.45 (0.46)	2.20 (0.65)	2.06 (0.71)	0.009
BDI (0-63) ^a	11.15 (8.41)	4.15 (3.51)	13.47 (7.51)	11.44 (7.79)	0.001
WT/pCO ₂	32.16 (4.79)	34.59 (4.98)	32.22 (3.98)	31.52 (5.41)	0.062
VH/pCO ₂ ^b	30.29 (5.05)	36.18 (4.22)	31.63 (4.33)	30.75 (9.05)	0.031
WT/RR	11.57 (5.03)	9.27 (4.10)	12.26 (3.15)	13.98 (3.57)	0.000
VH/RR ^c	11.82 (4.37)	9.21 (4.23)	11.68 (3.43)	12.68 (4.27)	0.004

^a N=16 for WL

^b N=18 for BT, N=16 for WL

^c N=19 for BT, N=16 for WL

Note: PDSS = Panic Disorder Severity Scale; SDS = Sheehan Disability Scale; ASI = Anxiety Sensitivity Scale; MI-ALL = Mobility Inventory (alone); BDI = Beck Depression Inventory; WT/pCO₂ = resting pCO₂ after walking; WT/RR resting respiration rate after walking, VH/pCO₂ = recovery pCO₂ after hyperventilation; VH/RR = recovery respiration rate after hyperventilation.

Table 2
Means, standard deviations, and significance of linear trends for questionnaire, diary, and physiological data: Across treatment weeks

Measures	Week 1	Week 2	Week 3	Week 4	<i>p</i>
<i>Session questionnaire</i>					
ASI (0-4) ^a	1.53 (0.70)	1.43 (0.70)	1.15 (0.58)	1.03 (0.64)	0.000
MI-AAL (1-5) ^a	1.83 (0.67)	1.80 (0.67)	1.72 (0.63)	1.65 (0.60)	0.008
BDI (0-63) ^a	8.00 (6.47)	7.00 (5.83)	5.76 (5.46)	5.76 (5.68)	0.036
<i>Daily ratings</i>					
Anxiety ratings (0-10) ^d	3.38 (1.88)	2.86 (1.69)	2.44 (1.68)	2.16 (1.56)	0.000
Depression Ratings (0-10) ^c	1.58 (1.91)	1.25 (1.33)	1.05 (1.26)	1.26 (1.29)	0.100
Worry ratings (0-10) ^c	2.58 (2.23)	2.17 (1.92)	1.84 (1.64)	1.57 (1.51)	0.000
<i>Physiological measures</i>					
<i>pCO₂</i>					
baseline ^b	36.67 (3.04)	36.76 (2.53)	37.23 (2.64)	37.88 (2.82)	0.008
paced ^d	34.69 (5.14)	36.70 (2.69)	37.56 (3.07)	38.75 (3.44)	0.000
transfer ^b	34.53 (5.03)	35.98 (2.71)	36.72 (3.07)	37.67 (3.66)	0.000
<i>RR</i>					
base ^b	14.75 (3.55)	14.08 (2.63)	12.74 (3.10)	12.23 (3.76)	0.001
paced ^d	12.95(0.93)	11.31 (1.57)	9.05 (1.50)	7.76 (23.61)	0.000
transfer ^b	13.30 (1.94)	11.77 (1.94)	9.85 (2.22)	8.52 (2.95)	0.000

^aN=34; ^bN=35; ^cN=32; ^dN=33

Note: ASI=Anxiety Sensitivity Scale; MI-ALL=Mobility Inventory (alone); BDI=Beck Depression Inventory; anxiety, depression, worry ratings=daily dairy mood rating for anxiety, depression and worry about panic; baseline=baseline pCO₂ or RR; paced=paced breathing plus capnometer feedback of pCO₂ or RR; transfer=only capnometer feedback of pCO₂ or RR. *p*= test of within contrast (linear trends). The average amount of exercises was 47.37 (SD: 9.56).

Table 3

Slope as outcome measure for clinical and respiratory measures: Pretreatment through follow-up

Measures	PDSS	SDS	ASI	MQ	BDI	WT/pCO ₂	WT/RR	VH/pCO ₂	VH/RR
Slope	-2.86	-3.20	-2.15	-0.52	-6.24	8.02	-6.76	15.49	-10.91
Z-score	-4.75	-3.63	-3.55	-4.01	-2.95	-1.87	-1.88	-2.60	-2.77
<i>p</i>	.000	.000	.000	.000	.003	.062	.060	.009	.006

Note. PDSS = Panic Disorder Severity Scale; SDS = Sheehan Disability Scale; ASI = Anxiety Sensitivity Scale; MI-ALL=Mobility Inventory (alone); BDI=Beck Depression Inventory; WT/pCO₂ =quite sitting pCO₂ after walking; WT/RR=quite sitting respiration rate after walking, VH/pCO₂=quite sitting pCO₂ after hyperventilation; VH/RR=quite sitting respiration rate after hyperventilation.

Table 4

Percentage of patients meeting the criteria for response/reliable improvement to treatment at posttreatment or 2-month follow-up, and remission/clinical significant change at 12-month follow-up

	Post		2FU	12FU
	BT (N=20)	WL (N=17)	BT (N=34)	BT (N=29)
PDSS_AS (RES ^a /REM ^b)	80 ^a	6 ^a	94 ^a	96 ^b
PDSS_AS (RI ^c /CSC ^d)	80 ^c	12 ^c	73 ^c	53 ^d
PA (zero)	40	6	62	68
CGI (? 3)	-	-	88	96

^abased on measures for response and ^bremission according to Shear et al. (1998)

^cbased on measures of reliable improvement or ^dclinical significant change by Jacobson et al. (1999)

Note: BT=treatment group, WL=waiting-list control, Post=posttreatment, 2FU=2-months follow-up, 12FU=12-month follow-up; PDSS_AS=Panic Disorder Severity Scale (avoidance and interference); panic attacks, CGI=Clinical Global Impression of Change; RES=response to treatment; REM=remission; RI=reliable improvement; CSC=clinical significant change;

Table 5

Correlations (r) between slopes (pretreatment through 12-month follow-up) for clinical ratings, self-report, and respiratory variables

Measure		WT/pCO ₂	WT/RR	VH/pCO ₂	VH/RR
PDSS	r	-.10	.31	-.33	.41
	p	.284	.033	.026	.007
SDS	r	-.10	.44	-.22	.50
	p	.276	.004	.097	.001
ASI	r	.05	.27	-.37	.24
	p	.394	.059	.015	.083

^a = one-tailed

Note. PDSS = Panic Disorder Severity Scale; SDS = Sheehan Disability Scale; ASI = Anxiety Sensitivity Scale; WT/pCO₂ = quite sitting pCO₂ after walking; WT/RR = quite sitting respiration rate after walking, VH/pCO₂ = quite sitting pCO₂ after hyperventilation; VH/RR = quite sitting respiration rate after hyperventilation.

Figure Legends

Figure 1. Mean scores and standard errors of end-tidal pCO₂ and respiration rate values across 4 treatment weeks. Dotted lines represent 2-minute baseline values prior to exercise, broken dotted lines represent 10-minute paced breathing values (capnometer and auditory feedback), and solid lines represent 5-minute transfer period (only capnometer feedback).

Figure 2. Mean values and standard errors of end-tidal pCO₂ and respiration rate values from pretreatment through 12-month follow-up. Solid lines represent quite sitting periods after walking, and dotted lines, quiet sitting values after voluntary hyperventilation.

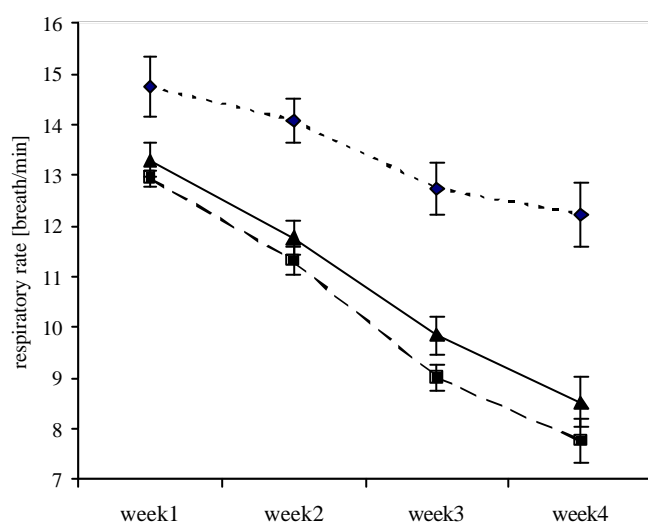
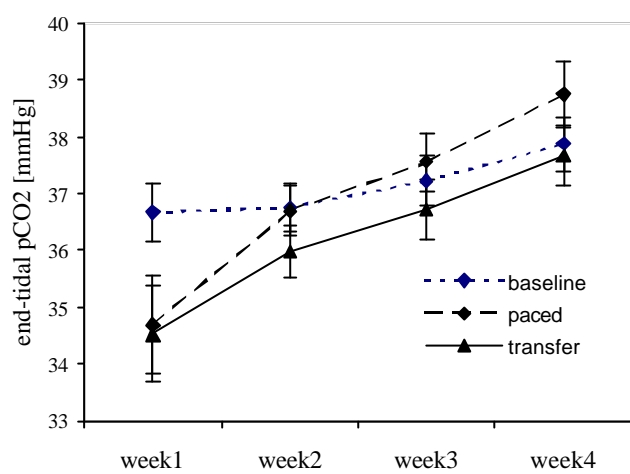
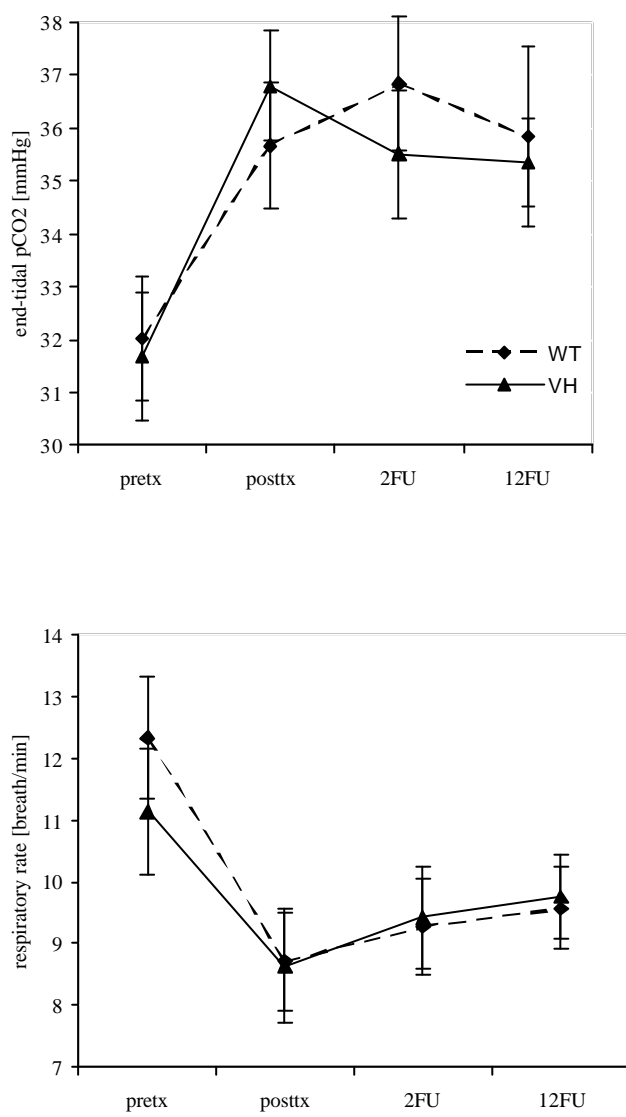
Figure 1

Figure 2

RESPIRATORY FEEDBACK FOR TREATING PANIC DISORDER: CONCEPT AND ILLUSTRATION

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ABSTRACT

Panic disorder patients often complain of shortness of breath or other respiratory complaints, which has been used as evidence for both hyperventilation and false suffocation alarm theories of panic. Training patients to change their breathing patterns is a common intervention, but breathing rarely has been measured objectively in assessing the patient or monitoring therapy results. We report a new breathing training method that makes use of respiratory biofeedback to teach individuals to modify four respiratory characteristics: increased ventilation (respiratory rate \times tidal volume), breath-to-breath irregularity in rate and depth, and chest breathing. As illustrated by a composite case, feedback of respiratory rate and end-tidal $p\text{CO}_2$ can facilitate voluntary control of respiration and reduce symptoms. Respiratory monitoring may provide relevant diagnostic, prognostic, and outcome information.

Keywords: panic disorder, breathing retraining, respiration, hyperventilation, biofeedback, psychophysiology.

Recurring episodes of intense physical sensations are characteristic of panic disorder. These symptoms are often respiratory, such as shortness of breath, tightness in the chest and difficulty in taking a deep breath, or are autonomic, such as a pounding heart and sweating (McNally, Hornig, & Donnell, 1995). Although panic disorder is currently diagnosed solely on the basis of subjective physiological symptoms, some researchers and therapists have sought ways to correct objective physiological disturbances that may underlie the development or maintenance of this disorder.

Theoretical Foundations

Cognitive-behavioral therapy (CBT) has achieved the status of the most accepted psychological treatment for panic disorder. A primary goal of CBT is to change catastrophic misappraisal of bodily sensations, often those apparently related to hyperventilation. These sensations can become part of a conditioned fear reaction (Barlow, 2002). At a cognitive level, CBT aims to reverse faulty attitudes and misperceptions through education. The patient learns about the fight-flight response and the physiology of the anxiety. Physiological symptoms of anxiety are taught to be normal and harmless. At a behavioral level, conditioned emotional responses are extinguished by prolonged exposure to these symptoms (exposure). In addition, the patient may learn to alleviate anxiety symptoms through relaxation and breathing training.

Treatment directed towards bodily symptoms and implicitly towards their physiological origin reaches back to the earliest CBTs, which accepted much of the hyperventilation theory of panic (Ley, 1985) and consequently accorded an important role to breathing training. Hyperventilation (overbreathing) is defined as a rate and depth of breathing that is too much for the body's need at that particular point in time. In its simplest form the hyperventilation theory posits a correspondence between arterial hypocapnia (low $p\text{CO}_2$) and anxious states. Acute hyperventilation is linked with panic attacks. Another, later theory of panic disorder also has a place for hyperventilation. According to the false suffocation alarm theory of panic (Klein, 1994), hyperventilation is an attempt to lower $p\text{CO}_2$ in order to avoid triggering a suffocation alarm that is overly

sensitive to pCO₂ elevation. Both theories find support in the high incidence of reported respiratory distress (especially dyspnea) during panic episodes.

In addition, research has found evidence for respiratory dysregulation in panic disorder, much of which is related to hyperventilation. Respiratory provocation tests (voluntary hyperventilation, CO₂-inhalation) are able to trigger panic attacks in many of panic disorder patients (Papp et al., 1997; Rapee, Brown, Antony, & Barlow, 1992). Panic patients show slower pCO₂ recovery after hyperventilation, and sometimes hypocapnia during extended baseline recordings (Wilhelm, Gerlach, & Roth, 2001a; Wilhelm, Trabert, & Roth, 2001b). Irregular respiration with frequent sighing is also characteristic of panic patients at baseline (Wilhelm, Trabert, & Roth, 2001). Finally, modification of respiration patterns reduces severity and frequency of panic attacks (Bonn, Readhead, & Timmons, 1984; Salkovskis, Jones, & Clark, 1986).

The success of CBT packages that include prevention of hyperventilation, together with research findings of respiratory irregularities in panic disorder patients, support the assertion that breathing is an important component of panic therapy. However, the value of breathing training has recently been challenged. Data from controlled clinical studies suggest that breathing training is either less potent than other CBT techniques (such as interoceptive exposure), or does not provide additional benefit beyond other techniques. However, as we discussed in a recent review (Meuret, Wilhelm, & Roth, in press), many breathing training studies have been flawed in terms of their experimental design, their specific goals for changing breathing, and their monitoring of change.

Treatment Principles

We have developed a new technology-facilitated treatment to correct commonly observed respiratory abnormalities in panic disorder (Meuret, Wilhelm, & Roth, 2001). This treatment is being tested in a study comparing 20 treated patients with 20 waiting list controls. Patients learn to breathe more normally while progress is monitored by feedback of their individual respiratory behavior. Since we want to determine the efficacy

of our breathing training method separate from other CBT procedures, we avoid any discussion of cognitive misinterpretations, but concentrate on modifying four respiratory parameters: increases in the rate and depth of breathing, breath-to-breath irregularity in rate or depth (including sighing), and chest breathing. We seek to normalize dysfunctional breathing patterns, reestablishing slow, shallow, and regular diaphragmatic breathing. In the short term, we expect this to lead to a better control of hyperventilation-related bodily sensations and, in the long term, to elimination of panic episodes.

Our patients are provided with a hand-held, battery-operated capnometry device (Capnocount, Weinmann, Inc., Germany) to use while doing the breathing exercises outside the clinic. This device is currently not FDA approved but can be used in research applications. It helps patients understand and change their respiratory physiology on the basis of objective physiological information rather than subjective feelings. It continuously samples and quantifies CO₂ in the expired air via a nasal cannula, and displays the end-tidal pCO₂ of single breaths and the respiratory rate on a monitor. This information is stored in the device in a memory chip along with a time and date stamp. Stored data can be downloaded to a personal computer from where the data can be printed out as graphs (see Figure 1 a-c) for review at the weekly treatment sessions. This provides both patient and therapist objective information about changes in respiratory patterns. The time stamp works as an incentive for patients to comply with homework.

As a guide for homework, patients are provided with a portable tape recorder for playing back a timed tape-recorded sequence of pacing tones that model a regular and slow breathing pattern. In addition, patients are given daily rating forms on which to report their symptoms and emotions before and after the exercises and at the end of the day. They also receive a panic attack diary to rate frequency and severity of panic attacks.

As part of our assessment, patients undergo a 24-hr ambulatory physiological monitoring before therapy, and a second ambulatory monitoring after the final treatment session. The initial assessment is used to explore individual aspects of the patient's breathing patterns that need to be targeted, such as irregularities, sighs, or very fast and

deep breathing. Therapy comprises five individual treatment sessions over four weeks. Each weekly session, conducted by a psychologist, lasts 60 to 90 minutes. The first session is dedicated to a discussion of the treatment rationale, the outcome of the 24-hr pretreatment physiological monitoring, a demonstration of the capnometer and how different breathing patterns affect it, and homework assignments. In each of the following sessions, the therapist and patient discuss printouts of pCO₂ and respiratory rate during the home breathing exercises, self-reports from these exercises, and the daily mood rating forms and panic attack records. Follow-up appointments are scheduled eight weeks and 12 months after termination of treatment.

Case Study

Presenting Problem and Client Description

The following description is not of a single patient, but a composite of several patients, thus preserving patient anonymity and enabling us to introduce a greater variety of reactions to therapy.

Jane was a 48-year-old divorced woman who presented at the first author's office concerned about various physical symptoms that she experienced during panic attacks. She had been working for some years in a personnel department. Four years before, she had been advised by her medical doctor to take a two-month sick leave because of physical and psychological exhaustion. During that leave she reduced her dose of diazepam, which had been prescribed for severe migraines, and went into psychotherapy, where her long-standing problems with the relationship with her father were addressed. She felt these problems had been making her depressed. When Jane came to us, she was on a second sick leave, this time because of severe panic attacks and agoraphobia. She was not on any medication.

Jane's panic disorder started shortly after she returned to work following her first sick leave. She said that her worst panic attack was at a dinner reception that she had organized for her company. When leaving an elevator with some guests, fear suddenly

overwhelmed her. Her heart was racing, she felt lightheaded and short of breath, and her chest was tight, making her feel that she was suffocating. She developed an intense feeling of unreality and began to worry she might be having a heart attack. She managed to leave the setting, feeling humiliated and helpless. After this event Jane had recurrent panic attacks, mostly at night. She would wake up in terror with her heart racing, covered with sweat, and unable to catch her breath. She would lay awake for hours unable to fall back asleep. Her greatest concern was that she might suffocate. She related this to traumatic events during her childhood. Several times her father had grabbed her around the neck to punish her for misbehavior. Ever since then she had been unable to have anyone get close to her neck or nose; even wearing turtleneck pullovers evoked feelings of suffocation. She also avoided closed places, such as elevators or windowless rooms. When driving, she would always keep her window open to get plenty of fresh air to breathe. Jane's fear of panic attacks had impaired her ability to function in social settings, which was essential for her job. Her fear and avoidance increased rapidly along with a feeling of exhaustion to the point that she had decided to quit her job.

Case Formulation

At the initial appointment Jane underwent a thorough diagnostic assessment. We evaluated the current levels of anxiety and avoidance by having Jane fill out several self-report measures.

Jane met DSM-IV criteria for panic disorder with moderate agoraphobia. During the prior month, Jane had experienced an average of three panic attacks with four or more symptoms per week and several with fewer symptoms per week. Her most common symptoms were heart racing and shortness of breath. She rated many of her panic attacks as being extremely disabling in that at night they would keep her awake for hours or during the day she have to leave the place where they occurred (usually crowds and places that seemed to have less fresh air). Jane also experienced severe anticipatory anxiety, often preventing her from entering feared situations. As a result of the nocturnal panic attacks, she had changed her sleep schedule to stay awake longer. When she was exhausted, she could fall asleep rapidly without lying awake and worrying about having

another panic attack. In addition, she avoided sleeping away from the relative safety of her home.

Course of Treatment

During the first half of the initial treatment session, the therapist educated Jane about panic disorder and the role of breathing. Psychophysiological explanations of the origin and maintenance of panic were presented, emphasizing hyperventilation and its possible impact on feelings and physiology. Topics were the fight-flight response, what triggers it and its immediate effects on the body, the physiology of breathing and hyperventilation, and how aberrant breathing patterns in panic disorder can be modified. Jane expressed great interest in physical symptoms that might accompany the fight-flight response. She found explanations of physiological changes during acute hyperventilation that lead to symptoms like heart racing and feelings of suffocation, particularly illuminating.

Following discussion of the treatment rationale, we turned to the results of her first 24-hr ambulatory monitoring. This had involved wearing a light multichannel physiological recorder in a waist pack. Channels included the electrocardiogram, respiration via non-restrictive elastic cotton belts, skin conductance, and the partial pressure of end-tidal carbon dioxide ($p\text{CO}_2$). PCO_2 is measured from air sucked with a miniature electric pump from prongs in each nostril through a transparent tube into the measuring device. For this to be accurate, clients have to be breathing through their nose.

As Jane reported later, the monitoring was a “real eye opener” to her in many ways. First, she had doubted she would be able to wear the nasal cannula for 24 hours because she thought it would make her feel that she was suffocating. However, those feelings wore off after the first 15 minutes of the recording. She was also able to let the therapist attach a voice sensor on her throat and keep it on for the complete period. Thus, the monitoring was form of exposure with unplanned positive effects: She found that something in her nose and on her throat, although initially frightening, was no longer so after a few minutes. The therapist went over the recordings and showed Jane her $p\text{CO}_2$ levels and breathing activity during various recording periods (day vs. night), activity

states (sitting vs. walking), and locations (at home and outside). We discovered that Jane's respiratory pattern was often that of erratic, deep (in the sense of high volume, not deep in the abdomen), chest breathing albeit at a moderately high rate. During the night, her breathing patterns were more regular but interrupted by occasional sighs. Her pCO₂ levels were chronically lowered throughout the day and night (30 mmHg vs. normal 37-40 mmHg). Our conclusion after examining the record together was that the training should focus on the establishment of regular, shallower breathing, with special attention to eliminating sporadic deep inhalations (sighing, yawning, and gasping for air).

We had asked Jane, as we do all of our patients, to do a hyperventilation test according to a specific procedure five times during the 24 hours. In examining the data, Jane made the connection between continuation of panic symptoms after the test and continued but unintended hyperventilation, documented by persistently low pCO₂ levels. As were many patients, she had felt very anxious, breathless, dizzy with her heart pounding during the test, and these feelings had persisted throughout the eight-minute recovery period. The pCO₂ recordings gave a convincing explanation for their persistence.

The second half of the first treatment session was devoted to breathing techniques and the homework assignments. We began by teaching abdominal breathing, Jane placing one hand on her abdomen and the other on her chest. After she was able to breathe evenly with most of the movement in the abdomen, she was encouraged to decrease the volume of her inhalations. After a few minutes she signaled feelings of shortness of breath, which she immediately tried to compensate for with larger gasps of air. She felt that if she continued to breathe shallowly she would suffocate. To test Jane's assumption, the capnometer was consulted for evidence and, contrary to her assumptions, displayed below normal pCO₂ levels, indicating that Jane continued to inhale more air than her body actually needed. This is the conversation we had in which we discussed the breathing techniques:

Therapist: Okay, so what I want you to do is to decrease the amount of air you inhale.

You can do that by imagining that you're breathing through a straw. Very little air gets through the straw, so if you feel much air flowing at your nostrils, you are probably taking in too much air. Let the air flow in and out of your nostrils quietly without forcing it, without feeling any resistance to the flow anywhere.

Jane: I understand what you're saying, but honestly, it scares me to cut down on my breathing. It makes me feel as if I'm suffocating. Pressure on my chest seems to increase, and I feel I have to take a deep breath.

Therapist: Well, why don't you take a deep breath and we'll see what happens to your CO₂ and to how you feel.

Jane: Hmmm. I felt a moment of relief, but now I feel even more out of breath. Why is that?

Therapist: Taking deep breaths leads to an abrupt reduction of CO₂ in the blood. The body reacts to this loss by sending you an alarm in form of symptoms of hyperventilation like dizziness or shortness of breath. The feelings are deceptive, since even though you took in too much air, you feel as if you didn't get enough. These feelings frighten a lot of panic patients and make them breathe deeper and faster, causing even more body symptoms. They end up making their symptoms worse instead of better.

Jane: Yes, that's exactly what happens to me. So, you're saying I shouldn't take a deep breath and should breathe shallowly even if I feel that I'm not getting enough air.

Therapist: Correct. Initially, that will be hard, since you'll have to overcome the urge to breathe deeper to compensate for feeling out of breath. That's where the Capnocount will help. It shows exactly what your physiological state is in terms of CO₂ levels and respiratory rate. Using it, you can learn to make your breathing healthier and ultimately more satisfying.

This conversation is typical of the attitude panic patients have towards their respiratory sensations and breathing. Jane felt that the explanations were helpful, but had great difficulty in controlling the rhythm, speed, and depth of her breathing. To support her efforts in pacing her breathing, the therapist introduced a training tape. Jane was

given the goal of following a tone with rising (inhalation) and falling (exhalation) pitch. Regulating her breathing rate and rhythm according to this external aid brought immediate relief. In a little while she felt more confident that she could maintain an even breathing pattern while decreasing her inspiratory volume and raising her pCO₂ levels on the display.

As the last part of the initial session, Jane was instructed in how to perform daily breathing exercises. The homework instructions were detailed: Twice daily she was to do the exercises using the Capnocount. In the first week, Jane was to follow a recorded tone sequence corresponding to a respiratory rate of 13 breaths per minute. In weeks 2 to 4, respiratory rates of 11, 9, and 6 breaths per minute were prescribed. Each 17-minute exercise consisted of three parts: (a) a baseline during which she was to sit quietly and relaxed with her eyes closed for two minutes; (b) a 10-minute paced breathing phase during which she checked her pCO₂ and respiratory rate every 30 seconds; and (c), a five-minute breathing phase without pacing tones during which she tried to maintain the healthy breathing pattern in absence of timing information, but with continued pCO₂ and respiratory rate biofeedback. The practice tapes provided instructions about what to do for each part. Self-report data of mood and panic symptoms were recorded in diaries prior to, and at the completion of, her daily breathing exercise, together with ratings of symptoms and emotions experienced during any panic attacks she had that day.

In the subsequent treatment sessions the central focus was on analyzing and discussing Jane's breathing exercises. The printouts of the physiological data from the exercises recorded during the previous week served as a powerful educational tool. Based on this information, the therapist was able to help Jane overcome any problems and improve her techniques. In addition, applying the new breathing skills in difficult situations was discussed, for example, while riding in an elevator or after waking up with panicky feelings.

The two figures below taken from Jane's week 1 recordings were the topic of discussion at the second session.

Therapist: Let me explain what you see on the first printout. This is the first exercise you did (Figure 1a). The printout contains the date and the time of the exercise so we can easily compare it with symptoms and emotions you reported in your dairy. The upper line is your pCO₂ level over the course of the 17 minutes exercise while the lower line is your breathing rate. Remember, the exercise had three phases, a 2-minute baseline, 10 minutes of breathing with the tones, and 5 minutes of breathing without any tones. Look at the exercises you did during the last week, and tell me your overall impression.

Jane: Well, first of all the initial exercises look pretty messy. What are all these spikes?

Therapist: The spikes are breaths that were irregular in terms of speed and depth. If you look at exercises later in the week (Figure 1b), there are hardly any spikes, indicating fewer sudden changes in rate or depth.

Jane: That's true, but it looks like my CO₂ is often quite low when I tried to follow the tones.

Therapist: Yes, this happens for almost everyone during the first week. The reason is pretty simple: If you look at your respiration rate baseline, you see that it's much higher than the speed at which the tones are set. Your breathing rate was about 18 to 22 breaths per minute while the tones are at 13 breaths per minute. So by lowering the respiration rate so drastically, you must have automatically overcompensated for the reduction in rate by taking much deeper breaths.

Jane: And why did that happen?

Therapist: Well, from the 24-hr monitoring we know that your daytime CO₂ level hovers around 30 mmHg. Do you remember when we looked at the monitoring, your respiratory rate was quite high at times...about 20 per minute in times when you were not active? Often, if you make yourself breathe slower, you begin to feel out of breath. That's the reason it's important to check your CO₂ levels until you learn how to keep your rate down. If you see your CO₂ dropping, you know you're taking in too much air. Over time you'll overcome those feelings of suffocation and will realize that you actually don't have to breathe so much to get enough air.

Jane: I realize that whenever I focus on my CO₂ levels like in the first exercise, my breathing rate seems to get out of control, and when I focus on my rate, my CO₂ is off.

Therapist: Yes, the first week is difficult, but you'll see that your body will get used to the new pattern and with practice it'll become easier.

For the remainder of the treatment we continued in a similar manner to help the client progressively alter her breathing pattern, and using her new skills, to enter agoraphobic situations with more confidence. The following conversation is from the fourth session.

Therapist: How did it go last week in terms of panic attacks or avoiding things?

Jane: There was only one situation where I felt panic coming on.

Therapist: When was that? What symptoms did you have?

Jane: I decided to go to Wal-Mart after I hadn't been there for long time – maybe a year, and I had a very bad panic attack. I think it was because there aren't any windows and the air seems so stuffy. Anyway, the last time it happened, I had to leave my shopping cart and run out, imagining I would suffocate and faint. It was very embarrassing.

Therapist: I can imagine how stressful that must have been. How was it this time?

Jane: I guess this time I really wanted to test myself and my ability to control my physiology. When I went into the store I was definitely nervous, but I was able to watch my breathing. I noticed that I started to hold my breath and then gasp for air with my mouth wide open. My heart was pounding a little harder, but I didn't feel suffocated. I just focused on breathing very regularly and shallowly through my nose. It's funny, but I can even hear the practice tones when I do that!

Therapist: That must help. What happened then?

Jane: I continued walking through the aisles, and I noticed that my physical symptoms lessened gradually, though I still felt a bit anxious.

Therapist: How long did your anxiety last?

Jane: I would say that the symptoms lasted about 2 or 3 minutes, and the anxiety about 10 minutes. By the time I finished my shopping, I felt relaxed and even happy. The techniques have really given me an insight how reactions of the body can lead to

panic. Most importantly I have learned an effective tool for stopping panic in its tracks.

Outcome and Prognosis

Over the weeks of therapy, Jane improved steadily. Her panic symptoms had decreased markedly. She was not only approaching fearful situations more often, but she also experienced fewer and fewer physical symptoms in those situations. Jane's progress was visible in one of the last exercises of her fourth treatment week (Figure 1c). Her $p\text{CO}_2$ levels had normalized, her breathing rhythm and volumes were quite stable throughout the exercise, most importantly during the two-minute baseline when her breathing was not paced.

We had two follow-up appointments with Jane, one at two months and one at 12 months. At both times we briefly monitored her respiration. At two months, Jane reported one mild attack when visiting a cave in Northern California, but she didn't have to leave the cave prematurely. Her feelings of suffocation had lessened to the point that she could wear tight pullovers, use elevators without hesitation, and not recoil when her partner touched her neck. Her baseline $p\text{CO}_2$ levels and respiratory rates remained at healthy levels, and were also more stable in terms of respiratory rate and depth. She sighed much less frequently. At 12 months follow-up, Jane had not had any additional daytime or nighttime panic attacks despite the fact that her life had been quite stressful. She was working as a manager of a small company and felt confident in her position. Her monitored respiratory physiology remained normal. She reported that since her last visit she had paid attention to her breathing only when she started to feel nervous or developed anxiety sensations. Then she would make sure to breathe shallowly and with her mouth closed.

As stated earlier, our biofeedback-assisted breathing training focuses exclusively on changing aberrant breathing patterns. Nevertheless, Jane's responses to our questionnaires documented that her previously catastrophic beliefs about panic attacks and their symptoms had abated, and that her feeling of control over attacks had increased.

At the end of the therapy, Jane was proud of her ability to influence her physiology and – as a beneficial side effect - thereby control her thoughts and feelings. She felt that having been shown the initial physiological results of the 24-hour monitoring and of the breathing exercises had been essential in learning to overcome her panic and avoidance.

Clinical Issues and Summary

This composite patient exemplifies the panic symptomatology and respiratory characteristics of many patients. She started out with low levels of $p\text{CO}_2$ and reported dyspnea and heart racing. Her main strategy for coping with anxiety was to avoid sensations associated with panic or the situations in which they occurred. Her low $p\text{CO}_2$, irregular breathing and anxiety symptoms improved hand-in-hand over the course of therapy and follow-up. Jane's successful outcome is consistent with many of our other cases. The greater effectiveness of this treatment in 20 patients compared to 17 in a waiting-list group was highly significant statistically.

However, not all patients have Jane's respiratory characteristics. While some have chronically lower $p\text{CO}_2$ levels, others show normal levels, at least when not having panic symptoms. Often these patients manifest persistent breath-to-breath variability in rate and volume. Interestingly, these patients are sometimes aware of subtle changes in their respiration that they interpret as signs of a developing panic attack. For example, their sigh frequency may increase, and even these sporadic deeper breaths place them at risk for developing hypocapnia. Encouraging regular respiratory patterns is more important than changing the depth of breathing for these patients.

Of course, there are probably panic disorder patients without disordered respiration for whom breathing training would not be helpful. In our current study, we have enrolled panic patients regardless of whether they came in complaining of respiratory symptoms during panic attacks. Nevertheless, patients with few or no respiratory symptoms improved as much as patients with predominant respiratory symptoms. This may indicate that breathing training helps patients without breathing abnormalities by inducing a relaxed state through nonrespiratory physiological mechanisms or by some kind of

placebo response. However, the absence of reported respiratory symptoms cannot be taken as proof that respiration is normal, and unfortunately physiological measurement is still not reliable enough to be certain that a patient has no respiratory disturbances during attacks (Meuret, Wilhelm, and Roth, 2003).

Our initial results encourage us to recommend the use of a $p\text{CO}_2$ biofeedback monitor for enhancing the effectiveness of breathing training. The emphasis on respiration rate of previous breathing therapies may be ineffective: our experience suggests that a reduction in respiration rate often leads to a compensatory increase in tidal volume, which in turn can decrease $p\text{CO}_2$ even further and worsen hyperventilation. Patients often have been told by physicians, psychologists, and friends to “take a deep breath” when they feel panicky. Overcoming this ingrained notion can be extremely difficult without the credible evidence of numeric feedback of an electronic device.

Monitoring respiration should not only be an essential part of breathing training, but should be generally useful in CBT treatments of panic disorder. Measuring physiological parameters can make a significant contribution to understanding why treatment is successful and why it sometimes fails or the patient soon relapses. However, understanding how a physiologically-oriented therapy really works is a daunting problem because of the complex relationships between body and mind. It may be that the convincing rationale of our therapy is simply a powerful way to alter the negative expectations that maintain panic disorder, giving patients a sense of being able to control their physiology . This possibility can be excluded by comparing our therapy with other therapeutic procedures equally plausible and capable of giving panic patients a similar sense of control.

Whatever the outcome of future studies, our clinical experience suggests that this biofeedback-assisted panic treatment will be a valuable addition to the practitioner's toolbox. In addition to generally enhancing treatment, it is a way to reach potential clients who are highly focused on bodily symptoms and convinced that a physiological disturbance - and not their thoughts - is the underlying cause of their panic attacks. Such clients are often reluctant to enter a psychological treatment. An initial somatic approach

can establish rapport with these patients and serve as a bridge to other behavioral and cognitive techniques if those are indicated.

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FIGURES LEGENDS

Figure 1. Breath-by-breath end-tidal pCO₂ and respiratory rate (RR) printouts of exercises performed in the first (a, b) and last treatment week (c) over the course of the biofeedback breathing exercise. Upper line represents end-tidal pCO₂ and lower line represents respiratory rate. (A: baseline; B: paced breathing tones with pCO₂ feedback; C: only pCO₂ feedback)

