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 (PCO_2) 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 PCO_2 levels, increased those levels during therapy, and maintained those levels at posttherapy and/or follow-up. Partial dissociation between PCO_2 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 (PDSSS 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 × 128 × 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

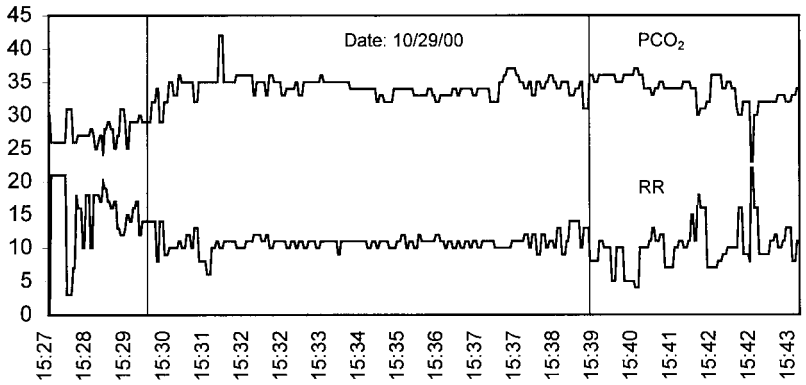

Figure 1. Printout of partial pressure of carbon dioxide (PCO_2) and respiratory rate (RR) capnometry recording for Patient 1, 2nd week, fourth breathing exercise.

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

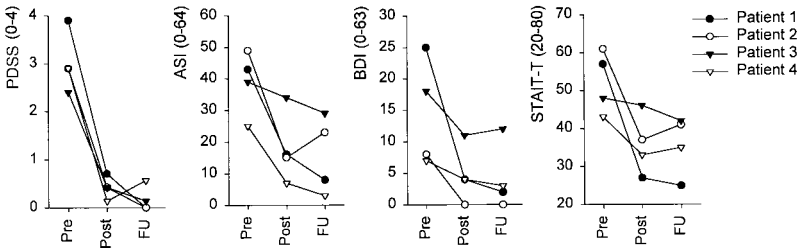

Figure 2. Individual scores for the clinician ratings (Panic Disorder Severity Scale) and questionnaires for Patients 1 to 4 during pretreatment (pre), posttreatment (post), and follow-up (FU) assessment.

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

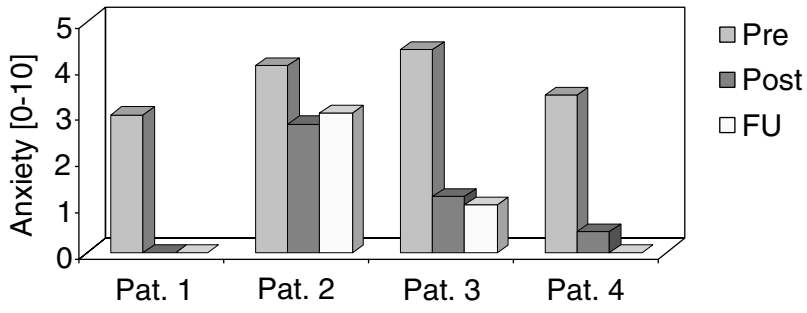

Figure 3. Individual anxiety scores during hyperventilation tests for Patients 1 to 4 during preassessment (pre), postassessment (post), and follow-up (FU) assessment.

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

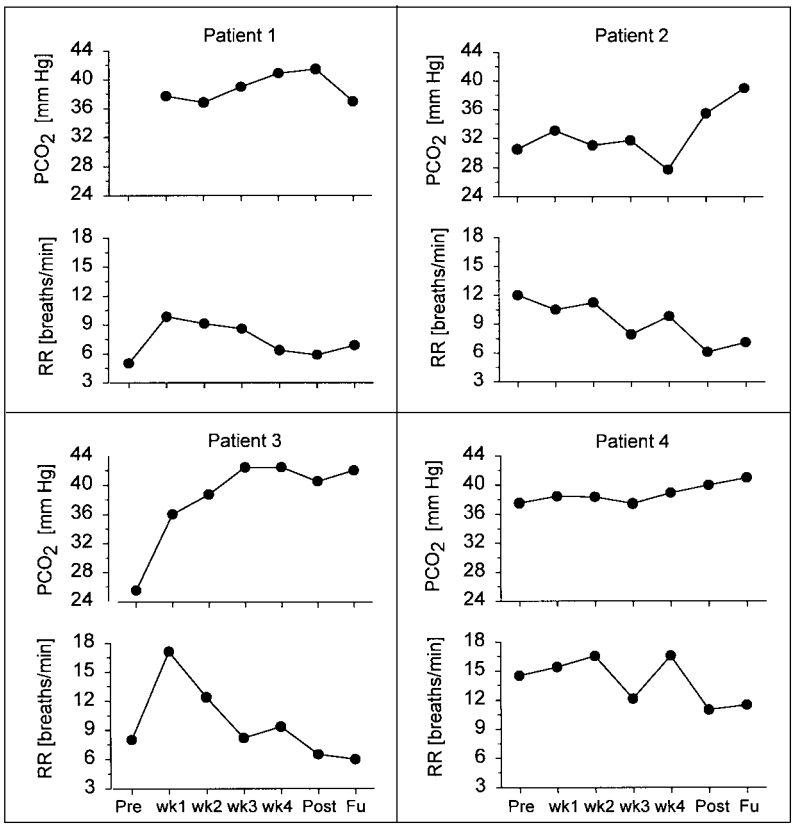

Figure 4. Individual levels of end-tidal partial pressure of carbon dioxide (PCO_2) and respiratory rate (RR) for Patients 1 to 4 from preassessment through follow-up (FU) assessment.

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, PCO_2 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

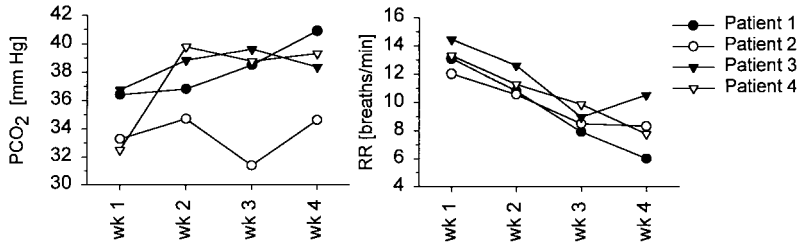

Figure 5. Individual levels of end-tidal partial pressure of carbon dioxide (PCO_2) and respiratory rate (RR) for Patients 1 to 4 during therapy, while performing paced breathing.

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, PCO_2 increased across weeks, and RR decreased. Increases in PCO_2 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 PCO_2 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. PCO_2 at Week 4 was raised above levels of Week 1 in Patients 1, 3, and 4. However, successive increments in PCO_2 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.

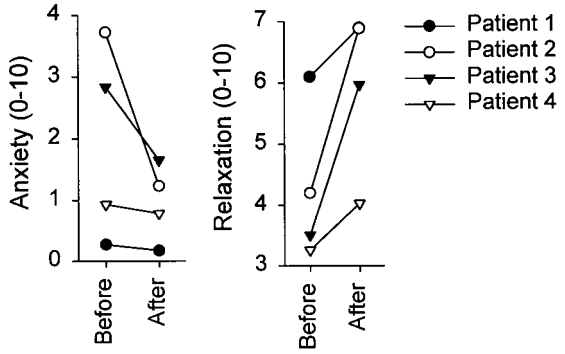

Figure 6. Individual anxiety and relaxation scores before and after breathing exercises (averaged over 4 weeks) for Patients 1 to 4.

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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