Voluntary hyperventilation in the treatment of panic disorder—functions of hyperventilation, their implications for breathing training, and recommendations for standardization

Alicia E. Meuret\textsuperscript{a,}\textsuperscript{*}, Thomas Ritz\textsuperscript{b}, Frank H. Wilhelm\textsuperscript{c}, Walton T. Roth\textsuperscript{d}

\textsuperscript{a}Center for Anxiety and Related Disorders at Boston University, United States
\textsuperscript{b}Psychological Institute III, University of Hamburg, Germany
\textsuperscript{c}Department of Psychology, University of Basel, Switzerland
\textsuperscript{d}Stanford University and The Veterans Affairs Palo Alto Health Care System, United States

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Abstract

Hyperventilation has numerous theoretical and empirical links to anxiety and panic. Voluntary hyperventilation (VH) tests have been applied experimentally to understand psychological and physiological mechanisms that produce and maintain anxiety, and therapeutically in the treatment of anxiety disorders. From the theoretical perspective of hyperventilation theories of anxiety, VH is useful diagnostically to the clinician and educationally to the patient. From the theoretical perspective of cognitive–behavior therapy, VH is a way to expose patients with panic disorder to sensations associated with panic and to activate catastrophic cognitions that need restructuring. Here we review panic disorder treatment studies using breathing training that have included VH. We differentiate the roles of VH in diagnosis, education about symptoms, training of breathing strategies, interoceptive exposure, and outcome measurement—discussing methodological issues specific to these roles and VH test reliability and validity. We propose how VH procedures might be standardized in future studies.

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1. Introduction

Hyperventilation has a long history of being linked to anxiety. Breathing-related symptoms such as dyspnea,¹ shortness of breath, or feelings of suffocation are central features of the experience of panic. This is reflected in the criteria for panic disorder in the Statistical Manual for Psychiatric Disorders (DSM-IV; American Psychiatric Association, 1994). Additional symptoms on this list are dizziness and tingling sensations in the extremities, both of which are typically produced by hyperventilation-induced alkalosis.² Subjective anxiety has been associated with hyperventilation³ both in individuals suffering from anxiety disorders and in those who do not (e.g., Rapee & Medoro, 1994; Rapee, Brown, Antony, & Barlow, 1992). These links have motivated researchers to examine in a variety of experimental subjects what happens when hypocapnia⁴ is produced by voluntary hyperventilation (VH) (Antony, Brown, & Barlow, 1997; Gorman et al., 1994; Holt & Andrews, 1989; Nardi, Valenca, Nascimento, & Zin, 2001; Papp et al., 1997; Spinhoven, Onstein, Sterk, & le Haen-Versteijnen, 1992; Wilhelm, Gerlach, & Roth, 2001). Two prominent psychophysiological models of panic, the hyperventilation model and the false suffocation alarm model, have assigned to abnormalities in respiratory gas exchange a central role in the development of panic and its maintenance (see Roth, Wilhelm & Pettit, in press; Smoller, Pollack, Otto, Rosenbaum, & Kradin, 1996, for a review).

The hyperventilation model of panic disorder (PD) assumes that at some time in the learning history of the patient, symptoms elicited by hyperventilation led to fear that in turn fuelled further hyperventilation, creating a vicious circle spiraling upwards to panic (Ley, 1985). Although it has been difficult to prove the etiological role of hyperventilation in panic (Roth, Wilhelm, Pettit & Meuret, in press), a number of findings support its relevance. These include lower basal pCO₂⁵ levels (e.g., Papp et al., 1997; Roth, Wilhelm, & Trabert, 1998; Salkovskis, Jones, & Clark, 1986), stronger psychological response to VH (e.g., Antony et al., 1997; Gorman et al., 1994; Holt & Andrews, 1989), and slower recovery from VH (Gorman et al., 1988; Maddock & Carter, 1991; Wilhelm, Alpers, Meuret, & Roth, 2001) in patients suffering from PD compared to healthy controls. Respiratory abnormalities such as disorganized breathing patterns or frequent sighing have also been observed in individuals with panic disorder (Abelson, Weg, Nesse, & Curtis, 2001; Martinez et al., 1996; Stein, Millar, Larsen, & Kryger, 1995). A specificity of these abnormalities for panic and not other anxiety disorders was evidenced in some studies (e.g., Wilhelm et al., 2001; Wilhelm, Trabert, & Roth, 2001a, 2001b).

However, not all results support the hyperventilation model. Hypocapnia can be absent in individuals with panic disorder during baselines⁶ (Holt & Andrews, 1989; Woods et al., 1986), and even during naturally occurring panic attacks (Garssen, Buikhuizen, & van Dyck, 1996; Hibbert & Pilsbury, 1988). Van den Hout et al. (1992) observed hypocapnia at baseline with further decreases during an exciting

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¹ Dyspnea is defined as abnormal or uncomfortable breathing in the context of what is normal for a person according to his or her level of fitness and exertional threshold for breathlessness.

² Respiratory alkalosis is a condition of excessive alkalinity of arterial blood, most often associated with respiratory (breathing) disorders. The pH (a measure of acidity or alkalinity) is high and carbon dioxide levels are low.

³ Hyperventilation (overbreathing) is defined as a combination of rate and depth of breathing that is too much for the body’s needs at a particular point in time.

⁴ Acute decreases in arterial pCO₂.

⁵ Partial pressure of arterial blood carbon dioxide.

⁶ Quiet sitting periods.
film or fearful imagery in both persons with PD and non-PD anxiety disorder patients and these levels corresponded to levels of subjective distress, as compared to healthy controls. They interpreted the changes in end-tidal pCO₂\(^7\) as an effect of fear or excitement rather than their cause. A general conclusion from the experiments cited above is that hyperventilation, if present, is not specific to PD patients.

The false suffocation alarm model of PD postulates a role for hyperventilation but a different one from the hyperventilation model. Patients hyperventilate to achieve a persistent hypocapnic state at a safe distance below the threshold of their overly sensitive biological suffocation alarm (Klein, 1993). While the hyperventilation theory postulates that anxiety is caused by hypocapnic breathing, Klein’s theory postulates that hyperventilation serves as a way to avoid the anxiety caused by hypercapnic breathing. Support for this model comes from studies that showed exaggerated responses of people with PD to inhalation of gas mixtures with higher than room air CO₂ levels (e.g., Gorman et al., 1994; Rapee et al., 1992) and that found greater sensitivity of chemoreceptors\(^8\) in these individuals (e.g., Lousberg, Griez, & van den Hout, 1988). Some studies, however, have not reported PD-specific hypersensitivities or lower thresholds for rises in ventilation during rebreathing tests (e.g., Katzman et al., 2002; Schmidt, Telch, & Jaimez, 1996). A general criticism of these inhalation studies is that the CO₂ concentrations given are higher than those occurring naturally (McNally, Hornig, & Donnell, 1995).

Cognitive and behavioral models of panic also assign a role to hyperventilation. According to them, symptoms of hypocapnia tend to be misinterpreted and catastrophized by patients with PD as signs of impending, dire harm. These misinterpretations of bodily sensations lead to a positive feedback loop between anxiety and physical sensations, eventuating in full-blown panic attacks (Clark, 1986; Reiss & McNally, 1985). In cognitive–behavior therapy, VH serves as a convenient way of exposing individuals with PD to some of their panic symptoms (interoceptive exposure) and to the activation of catastrophic thoughts.

Given the theoretical interest in the link between hyperventilation and anxiety, it is not surprising that VH has often been employed in therapies. One of the attractions of respiration as a therapeutic focus is that, unlike autonomic anxiety responses, respiration is subject to conscious control. VH has the potential of voluntarily creating a state that is presumed to occur, and is sometimes observed to occur, without conscious intent, during states of anxiety, panic, and other emotions.

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. Fig. 1 shows the progression of a VH challenge performed in our laboratory with a panic patient (Meuret, Wilhelm, & Roth, 2002). After approximately 1 min, the patient met our prescribed criteria of lowering pCO₂ levels to 20 mm Hg at a respiratory rate of 18 breaths/min. After 3 min of VH, the patient stopped her efforts at hyperventilation, and her pCO₂ began to return to its initial level. Drops and spikes indicate irregularity in the breathing patterns such as sighs or pauses.

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

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\(^7\) Partial pressure of arterial blood carbon dioxide collected from the nose via nasal cannula.

\(^8\) Central and peripheral chemoreceptors participate in the control of ventilation by detecting short-term (acute) and long-term (chronic) alterations in blood gases (pO₂, pCO₂, and pH).
by the end of an 8-min recovery period, but in some patients, physical symptoms, anxiety, or feelings of unreality can persist.

2. Voluntary hyperventilation in panic disorder treatment (example breathing training)

Below we examine ways that VH has been applied clinically in order to examine further its role in clinical diagnosis, education about symptoms, breathing training, interoceptive exposure, and outcome measurement. Since most applications of VH are linked to breathing training (BT), we will exemplify various roles of VH using studies that have focused on testing BT effects. The rationale for conventional BT is to eliminate persistent or acute decreases in arterial pCO2 by means of slow, diaphragmatic breathing, and thereby prevent anxious states. This rationale is based on a hyperventilation model of panic disorder. BT has also been included as a component of cognitive–behavioral treatment packages (e.g., Craske, Barlow, & Meadows, 2000), often with an interoceptive exposure rationale. In this context, BT has also come under criticism of being counterproductive, as we will discuss later.

We identified nine published studies with BT as the sole therapeutic modality, or that emphasized BT in combination with few other components in designs where inferences about its efficacy as a separate component could be made (Bonn, Readhead, & Timmons, 1984; Clark, Salkovskis, & Chalkley, 1985; Craske, Rowe, Lewin, & Noriega-Dimitri, 1997; Franklin, 1989; Hibbert & Chan, 1989; Meuret, Wilhelm, Ritz, & Roth, submitted; Rapee, 1985; Salkovskis et al., 1986; Schmidt et al., 2000) (Table 1). BT instructions typically emphasized slow and abdominal breathing. 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 CBT packages (Craske et al., 1997; Schmidt et al., 2000). All of these studies included VH in one form or
<table>
<thead>
<tr>
<th>Study</th>
<th>BT treatment (n)</th>
<th>Type of BT technique</th>
<th>Control (n)</th>
<th>Type of BT outcome measures</th>
<th>Results for BT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonn et al. (1984)</td>
<td>2 sessions/2 weeks (plus seven weekly sessions of in vivo exposure) (7)</td>
<td>Slow and diaphragmatic breathing</td>
<td>Exposure only (5)</td>
<td>Psychological and physiological</td>
<td>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</td>
</tr>
<tr>
<td>Rapee (1985)</td>
<td>3 sessions/4 weeks (1)</td>
<td>Diaphragmatic breathing and reduction of respiratory rate and habitual sighing and yawning</td>
<td>–</td>
<td>Psychological</td>
<td>Decrease in panic attack frequency and severity, symptoms, and anxiety</td>
</tr>
<tr>
<td>Clark et al. (1985)</td>
<td>2 sessions/2 week (18)</td>
<td>Slow and regular breathing supported by audiotape</td>
<td>–</td>
<td>Psychological</td>
<td>Reduction in panic attack frequency and self-reported anxiety and depression after 2 weeks of training. Reduction in panic attack frequency and self-reported anxiety and depression; increase of pCO2 to normal levels</td>
</tr>
<tr>
<td>Salkovskis et al. (1986)</td>
<td>4 sessions/4 weeks (9)</td>
<td>Slow and regular breathing supported by audiotape (12 breaths/min)</td>
<td>–</td>
<td>Psychological and physiological</td>
<td>Self-reported measures of anxiety improve equally in treatment and placebo groups. At posttreatment, observer but not self-report ratings indicated a greater improvement in patients receiving BT</td>
</tr>
<tr>
<td>Hibbert and Chan (1989)</td>
<td>2 sessions/2 weeks (plus 3 weeks of exposure in vivo) (21)</td>
<td>Paced breathing supported by audiotape</td>
<td>Placebo treatment (19)</td>
<td>Psychological</td>
<td>BT was superior in reducing panic attack frequency and severity, catastrophic cognitions, anticipatory anxiety, and behavioral measures of agoraphobia</td>
</tr>
<tr>
<td>Franklin (1989)</td>
<td>1 session/4 weeks (compared to IIR, CM and IR) (4)</td>
<td>Slow breathing (12 breaths/min)</td>
<td>Delayed treatment (4)</td>
<td>Psychological</td>
<td>Interoceptive exposure was more efficacious on certain measures than BT in combination with cognitive restructuring and in vivo exposure</td>
</tr>
<tr>
<td>Craske et al. (1997)</td>
<td>2 sessions/2 weeks (CBT: 12 session/12 weeks) (18)</td>
<td>Slow and diaphragmatic breathing</td>
<td>Interoceptive exposure (20)</td>
<td>Psychological</td>
<td>Active treatment groups improved 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</td>
</tr>
<tr>
<td>Schmidt et al. (2000)</td>
<td>2 sessions/2 weeks (CBT: 12 session/12 weeks) (21)</td>
<td>Diaphragmatic breathing</td>
<td>Delayed treatment (24)</td>
<td>Psychological</td>
<td>Major clinical severity measures, respiratory rate, and pCO2 improved substantially from pre- to post-therapy and remained stable or declined further at 12-month FU</td>
</tr>
<tr>
<td>Meuret et al. (submitted)*</td>
<td>5 sessions/4 weeks (20)</td>
<td>Capnometry-assisted BT targeting slow (13, 11, 9, and 6 breaths/min over course of 4 weeks), regular, diaphragmatic, shallow breathing patterns</td>
<td>Delayed treatment (17)</td>
<td>Psychological and physiological</td>
<td></td>
</tr>
</tbody>
</table>

BT=breathing training, RR=respiratory rate, IIR=in situ isometric relaxation, CM=cognitive modification, IR=imaginal rehearsal, CBT=cognitive-behavioral therapy, WL=waiting list control, FU=follow-up.

* More details about the methodology of this study can be found in Meuret, Wilhelm, and Roth (2001, 2004).
another. Surprisingly, although the target of the BT treatment is respiration and thus a physiological one, few studies measured breathing pattern or gas exchange as outcome variables.

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 greater efficacy of BT than 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 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 did not show a marked benefit of BT in panic disorder. A more complete description of these studies and conclusions about the efficacy of BT appears in Meuret, Wilhelm, Ritz, and Roth (2003). 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.

2.1. Voluntary hyperventilation procedures

In the BT studies we reviewed, the VH instructions, verification, and assessment of outcome varied widely (Table 2). Test durations ranged from 1 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.” Sometimes no specific instructions were reported. In some studies, volume was not mentioned; thus if patients panted shallowly, they may not have substantially lowered their arterial pCO₂, or, paradoxically, may even have increased it since none of the CO₂ deep in the lungs may have been exchanged with outside air. Target pCO₂ levels were specified only in our own study, where patients were required in a 3-min period to quickly reach a level of 20 mm Hg 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., submitted). 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 PD was lacking, partly because of the various 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 more time-efficient but also has disadvantages. Visual or tactile monitoring of the respiration of individuals in a group is 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 unmonitored clients may not comply with this out of fear of the symptoms and embarrassment about panicking in front of other people. When VH is used therapeutically, it is easier to respond to individual reactions and idiosyncratic beliefs about it in one-to-one setting. Data from individuals collected in a group setting cannot be treated as independent cases statistically, if responses in one patient can influence responses in others.
Table 2
Techniques of hyperventilation used in breathing training studies and other relevant quality criteria

<table>
<thead>
<tr>
<th>Study</th>
<th>Test duration</th>
<th>Breathing pattern</th>
<th>Target breathing rate</th>
<th>Occurrence in the therapy</th>
<th>Check of compliance with test instruction</th>
<th>Outcome criteria</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapee and Medoro (1994)</td>
<td>1 1/2 min</td>
<td>Not reported</td>
<td>25 breaths/min</td>
<td>Once prior to treatment</td>
<td>Not reported</td>
<td>Verbal symptom report and judgments of similarity to past PAs</td>
<td>Education about symptoms</td>
</tr>
<tr>
<td>Bonn et al. (1984)</td>
<td>3 min</td>
<td>Vigorous chest panting though mouth and nose</td>
<td>60 breaths/min</td>
<td>Once prior to treatment</td>
<td>RR and mode of breathing was monitored</td>
<td>Verbal symptom report and judgments of similarity to past PAs</td>
<td>Diagnosis; education about symptoms</td>
</tr>
<tr>
<td>Clark et al. (1985)</td>
<td>Approximately 2 min</td>
<td>Fast and deep breathing through mouth</td>
<td>Not reported</td>
<td>Once prior to treatment</td>
<td>Not reported</td>
<td>Symptom rating sheet and questionnaire about similarity to past PAs</td>
<td>Diagnosis; education about symptoms</td>
</tr>
<tr>
<td>Salkovskis et al. (1986)</td>
<td>2 min</td>
<td>Forced ventilation</td>
<td>Not reported</td>
<td>Repeated VH as part of first session and home work</td>
<td>Not reported</td>
<td>Symptom rating sheet and questionnaire about similarity to past PAs</td>
<td>Education about symptoms</td>
</tr>
<tr>
<td>Hibbert and Chan (1989)</td>
<td>Approximately 2 min</td>
<td>Fast and deep breathing through mouth</td>
<td>Not reported</td>
<td>Once in BT group in the first session, in the placebo group after the final assessment</td>
<td>Not reported</td>
<td>Symptom rating sheet and questionnaire about similarity to past PAs</td>
<td>Diagnosis; education about symptoms; training of breathing strategies</td>
</tr>
<tr>
<td>Franklin (1989)</td>
<td>Three times (standing, sitting, and lying), up to 1 1/2 min, with 30-s breaks</td>
<td>Not reported</td>
<td>18 breaths/min</td>
<td>Repeated VH as part of first session and home training</td>
<td>Not reported</td>
<td>Hyperventilation questionnaire</td>
<td>Education about symptoms; training of breathing strategies</td>
</tr>
<tr>
<td>Craske et al. (1997)b</td>
<td>1– 1 1/2 min</td>
<td>Fast breathing with hard exhalations</td>
<td>3 × faster than normal</td>
<td>Repeated VH as part of breathing training and interoceptive exposure</td>
<td>Not reported</td>
<td>Discussion with therapist about symptoms produced and judgment of similarity to past PAs</td>
<td>Education about symptoms; interoceptive exposure and extinction; outcome measure</td>
</tr>
<tr>
<td>Schmidt et al. (2000)c</td>
<td>1 min</td>
<td>Deep and fast breathing</td>
<td>Not reported</td>
<td>Repeated VH as part of interoceptive exposure</td>
<td>Not reported</td>
<td>Symptom intensity and similarity to past PAs</td>
<td>Interoceptive exposure and extinction</td>
</tr>
<tr>
<td>Meuret et al. (submitted)</td>
<td>3 min</td>
<td>Fast and deep</td>
<td>18 breaths/min</td>
<td>Repeated VH before and after treatment</td>
<td>Instructed reduction of pCO₂ to 20 mm Hg</td>
<td>Symptom rating and questionnaire about similarity to past PAs</td>
<td>Outcome measure</td>
</tr>
</tbody>
</table>

* The authors cite Clark et al. (1985) for the procedure of their VH test.
* Information retrieved from therapy manual (Craske, 1998).
How participants are prepared for VH is an important procedural variable that has varied between studies. Bonn et al. (1984) advised 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. On the other hand, certain prior information may increase anxiety. Compernolle, Hoogduin, and Joele (1979) warned their hyperventilation syndrome (HVS) patients that they might experience severe anxiety in order to increase the likelihood that VH would provoke panic in them, since the investigators felt patients would be most receptive to explanations of the rationale of therapy immediately after an 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 appear fraught with dangers, and make worriers worry even more.

2.2. Roles of voluntary hyperventilation in breathing training

An examination of what has been written about BT shows that VH has been given a number of distinct roles: diagnostic test, source of education about symptoms, teacher of breathing strategies, means of interoceptive exposure and extinction, and measure of outcome. In most studies that we reviewed, VH assumed more than one role.

2.2.1. Diagnosis

The central goal for BT in panic disorder is the reduction of hypocapnic breathing, but hyperventilation may not be characteristic of all individuals with PD. Historically, VH was used to diagnose HVS, a disorder which by definition was caused by repeated or sustained hypocapnic breathing. Such patients might complain of shortness of breath, light-headedness, chest pain, palpitations, or sweating, without apparent organic causes. Hypocapnia and disturbance of the acid–base balance were thought to be the origin of these symptoms (Lum, 1975). Although no general consensus about diagnostic criteria for HVS was reached, clinicians and researchers often employed a VH test for determining whether the patient’s symptoms were indeed due to hyperventilation (Bass, 1997). The parameters of the test were rarely standardized (Hornsveld, Garssen, & van Spiegel, 1995), but in general, patients were instructed to hyperventilate until symptoms occurred for periods from a few to 30 min, and these symptoms were then compared with the complaints for which patients sought treatment. Similarity was taken to mean that HVS was indeed the cause of the patient’s distress, in which case BT would be an appropriate treatment.

With the development of the current American Psychiatry Association classification of anxiety disorders, which does not include HVS, the suspicion arose that many patients diagnosed as having HVS would now be diagnosed as having PD. Consequently, VH was applied to patients meeting criteria for PD in the same way it was to presumed patients with HVS, namely, to identify a subgroup of individuals whose attacks are associated with hyperventilation and who might respond particularly well to BT. Like for HVS, this subgroup has usually been considered to be patients who respond to VH with self-reports of discomfort, anxiety, or panic. Some investigators have treated only patients who responded in this
way (Bonn et al., 1984; Clark et al., 1985), while others have used VH to identify a subgroup for assignment to a hyperventilation-oriented treatment module within their study (Hibbert & Chan, 1989).

Bonn et al. (1984) identified treatment candidates with their VH test: Participants had to breathe 60 breaths/min for at least 3 min 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 true ‘hyperventilators.’ Only 33% of their patients were able to complete the 3-min VH, and 20 of 21 met these criteria, whereas 96% of a healthy control group completed the test. The percentage of hyperventilators identified by Bonn et al. (1984) among candidate patients with symptoms of hyperventilation is high compared to that of Hibbert and Chan (1989), who identified 13 of 21 candidates 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.

Although using VH as a way of diagnosing the subgroup of individuals with PD who will respond to BT is intuitively appealing, it currently lacks empirical support for either its validity or its ability to predict the results of breathing training. First, if self-reports of hyperventilation symptoms are unrelated to actual physiological hyperventilation, then such symptom reports are irrelevant for BT. One study of HVS patients found self-report and physiological hyperventilation to be poorly correlated. Hornsveld, Garssen, Fiedeldij Dop, van Spiegel, and de Haes (1996) subjected patients with HVS symptoms to two hyperventilation procedures: one hypocapnic, lowering pCO2 by 50% of the baseline level, and one isocapnic, keeping pCO2 levels constant by addition of CO2 to the inspired air. Tests were administered double blind in random order. The authors found that patients were unable to distinguish between the two tests: symptoms elicited by the isocapnic VH were reported by almost half of the patients as symptoms occurring in their everyday life (‘symptom recognition’). Another 18% of the patients did not recognize their typical symptoms during either test. These results cast doubt on the validity of a VH test for diagnosing HVS and the validity of the HVS itself, if we accept the methodological claim that manual titration of 100% CO2 was fast enough and accurate enough to have prevented hypocapnic dips that could have triggered symptoms. One explanation of the results of isocapnic VH is that fast breathing had become a conditioned stimulus able to elicit symptoms that had occurred during previous episodes of hyperventilation. This experiment should be repeated with individuals diagnosed with PD since some of the patients tested by Hornsveld et al. may have had other diagnoses.

That initial VH predicts the outcome of BT has yet to be demonstrated. In our own study, described in more detail below under Outcome Measure (Meuret et al., submitted), we failed to find support for a relationship between pre-therapy response to a VH and subsequent outcome, even when controlling for initial levels for anxiety. The partial correlations between anxiety or shortness of breath during VH recovery and improvement in panic disorder severity, controlling for baseline anxiety, were r(32)=.05 and .11, respectively. However, we did not have patients rate the similarity of their VH-elicited symptoms to their panic attack symptoms.

If a VH test did predict BT outcome in PD, we would then wonder what incremental validity VH might have over reports of customary symptoms during panic attacks. We would suppose that BT would be more effective in patients with more respiratory symptoms. Our own results suggest that a predominance of respiratory symptoms did not predict better BT outcomes. On the other hand,
respiratory symptoms did predict better outcomes with tricyclic drug treatment of PD. In one study (Briggs, Stretch, & Brandon, 1993), the PD subgroup with prominent respiratory symptoms suffered more spontaneous panic attacks and responded better to imipramine than the subgroup without such symptoms, who suffered more situational panic attacks and responded better to alprazolam. In another study by Nardi et al. (2003), a respiratory subgroup showed a faster response to treatment with nortriptyline than did a non-respiratory subgroup, although overall improvement at posttreatment and follow-up did not differ between subgroups. This fits with the suffocation alarm model that postulates that patients with true PD, unlike patients with other anxiety disorders, are most likely to have respiratory symptoms during their attacks and are helped specifically by tricyclic antidepressants such as imipramine or nortriptyline (Klein, 1980).

Symptoms or physiological measures during VH might provide better predictive information than interviews or questionnaires assessing what the patient experienced in past attacks, but in order to test for incremental validity or to apply VH in other ways, standardization of VH is essential. The lack of a standard test may be why the percentage of identified hyperventilators varies so much between studies. The VH protocol of Bonn et al. (1984) is likely to elicit more intense and more varied panic symptoms than the protocol of Hibbert and Chan (1989), since Bonn et al. (1984) requires 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). The VH test of Hibbert and Chan (1989) required only 2 min of overbreathing. A critical parameter is likely to be the pCO2 level the patient reaches, yet only in one BT study were end-tidal pCO2 levels monitored and used as a performance goal (Meuret et al., submitted) (details of the method are in Wilhelm et al., 2001). Reliance on the most visible behavioral aspect of VH, breathing rate, is insufficient since patients can compensate for higher rates with reductions in tidal volume, thus avoiding more dramatic falls in pCO2 (Salkovskis et al., 1986). When tidal volume approaches respiratory dead space, typically about 160 ml in adults, arterial pCO2 can paradoxically rise even with very high respiratory rates because there is little gas exchange between the lungs and outside air. Goals for pCO2 levels and how long they are to be maintained must be established or more fearful patients will avoid hypocapnia by slower, shallower breathing.

Another aspect that has not been standardized is the assessment of symptoms experienced during the VH. Typically, intensity ratings for hyperventilation have been combined with some type of similarity rating between the VH experience and typical panic attacks. Two of the three studies used the same instruments for this purpose (Clark et al., 1985; Hibbert & Chan, 1989), but their criteria for identifying hyperventilators from it varied. Self-report criteria used by Bonn et al. (1984) were less standardized and strict, possibly explaining the high percentage of identified hyperventilators in their pre-treatment sample.

In order to use VH for diagnosis, the pCO2 level reached is unlikely to be the only parameter that needs to be taken into account, since symptoms and anxiety may also depend on the change from initial, pre-test pCO2 levels. Non-hyperventilators are more likely to begin the test with normal pCO2 levels than panic patients, who have hypocapnic levels (e.g., below 30 mm Hg; Bass & Gardner, 1985). Normocapnic participants would have to change more to reach a criterion of, say, 20 mm Hg, than would hypocapnic participants. Thus, if it is change that produces symptoms, VH to a fixed pCO2 criterion would be a weaker stimulus for patients who began the test with lower pCO2 values. Different initial values might distort measures of pCO2 recovery from VH as well. Change criteria, such as reduction of pCO2 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 to the subject about the physiology of the test and its possible effects is also likely to affect the diagnostic value. Emphasis on the unpleasantness of the symptoms may amplify anxious expectancy and reactions to the test, while information that is more neutral may make the symptoms 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 participants 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).

2.2.2. 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 varies. Franklin (1989) administered the VH test three times with varying body posture (standing, sitting, and 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 and 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 vary according to the theory behind the BT. An 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. This rationale can be a powerful agent for change. Bonn et al. (1984) reported 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. 668). Since patients are often unaware of hyperventilating if in fact they do, they might not accept the interpretation of their symptoms as hyperventilation-produced unless they experience the sometimes dramatic effect of VH reproducing their panic symptoms.

Cognitive–behavioral theoretical approaches, which emphasize the catastrophic misinterpretation of bodily symptoms, or symptoms becoming conditioned fear stimuli, use VH to teach a different lesson. Hypocapnic breathing, with its resulting symptoms, is portrayed 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 given to patients by Craske et al. (1997) as introductions to the first and second sessions, and as additional information in conjunction with the hyperventilation exercises in therapy. These investigators had patients hyperventilate in a group
of three to five patients for 1–1 1/2 min, after which patients sat with their eyes closed and were instructed to breathe very slowly, pausing at the end of each breath. Patients 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 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.

2.2.3. Teaching breathing strategies

VH can be used in therapeutic breathing training to help patients achieve greater control of anxiety and symptoms elicited by hypocapnia. Patients first hyperventilate and then apply the newly learned anti-hyperventilation breathing patterns (Franklin, 1989; Hibbert & Chan, 1989). They are told that controlling their breathing will help control their symptoms and should be applied during exposure or whenever they are anxious. Franklin (1989) instructed patients to repeat VH at least once a day and to employ the breathing control techniques as often as needed.

CBT protocols often use VH directly or indirectly to teach breathing strategies, although the protocol rationale may be education and interoceptive exposure. From an educational standpoint, if patients are able to trigger and then reduce fearful sensations simply by changing the way they breathe, then such sensations at other times must be a result of overbreathing and are therefore understandable, predictable, manageable, and harmless (Barlow, 2002). At the same time, even in the absence of explicit instructions, patients are being taught that, by breathing in certain ways, they can avoid anxiety. Advice to switch from thoracic to abdominal breathing to manage anxiety generated by interoceptive exposure during VH (Craske, 1998) is also a message about how to avoid anxiety at other times. If a new breathing strategy is reinforced by success, it is likely to be adopted by the patient regardless of the intention of the therapist. To what degree this occurs with specific CBT protocols is a question for research, one particularly relevant when the benefits of BT as an additional component of CBT are being tested (Schmidt et al., 2000).

2.2.4. Interoceptive exposure

VH has been used for interoceptive exposure with the aim of extinguishing fear of symptoms such as dizziness, shortness of breath, and heart racing by repeatedly having the client induce and experience these symptoms (Craske et al., 2000; Schmidt et al., 2000). VH is only one of a number of ways of eliciting feared symptoms: Others are rapidly turning around to induce vertigo, breathing through a narrow straw to elicit air hunger, and breath holding to induce feelings of suffocation. Exercises producing symptoms that rank high in patients’ ratings in their similarity to panic symptoms are repeated within sessions and at home. Therapists sometimes teach strategies of anxiety control to be applied immediately after anxiety is induced by VH. These strategies may be cognitive or directed to breathing (Craske, 1998).

From an exposure–extinction perspective, control strategies have the potential of being counter-therapeutic “safety aids,” since they might retard extinction by reducing exposure to the anxiety-provoking elements of the stimulus. From this perspective, if fear of breathing sensations is a symptom in panic situations, hyperventilation should be encouraged in these situations, not discouraged. This is one of the reasons that Craske et al. (1997) and Schmidt et al. (2000) conclude that BT does not contribute to, and may detract from, other psychological treatments of panic (see Meuret et al., 2003 for a more thorough discussion of this issue).
2.2.5. Outcome measure

To our knowledge, VH has been used only twice as an outcome measure (Craske et al., 1997; Meuret et al., submitted), which is surprising considering the widespread use of VH in behavioral PD treatments. Regardless of whether a treatment rationale considers hyperventilation itself or the cognitive misinterpretation of breathing sensations as central to the development of panic, psychological and physiological reactions to VH are eminently relevant to outcome. In the study of Craske et al. (1997), patients in both BT and interoceptive exposure groups performed a ‘behavioral approach test’ before and after treatment. This test included up to 1 min of overbreathing. Self-reports of anticipatory anxiety before the test and maximum anxiety during VH were collected. Few procedural details of the test were given and no statistical analysis, but judged by reported means, anxiety elicited by VH decreased equally in the two groups from pre- to post-therapy.

In our study, individuals with PD were assigned randomly either to receive immediate capnometry-assisted BT or to wait 4 weeks for treatment (Meuret et al., submitted). For the VH test, patients were instructed to breathe deeply to lower and maintain an end-tidal pCO2 of 20 mm Hg using an audiotape of tones to pace their breathing at a moderate speed of 18 breaths/min, while receiving visual pCO2 feedback from a capnometer. They were not told the purpose of the test nor about hyperventilation-induced panic beforehand. Panic-related symptoms (following DSM-IV criteria) and anxiety severity were rated before the VH challenge. After the challenge, patients were given 8 min to recover, after which they retrospectively rated their anxiety and symptoms for the hyperventilation and recovery periods. Physiological parameters such as respiration rate and pCO2 were measured continuously. This procedure was repeated several times over the day (some tests were conducted and recorded at home). The test battery was repeated after 4 weeks for both the group that had been treated (post-treatment) and for waiting list controls. The first VH of the post-assessment battery compared to the first VH pre-assessment battery showed higher pCO2 and lower respiration rates during recovery in the BT group than in the waiting-list group, even after controlling for changes in baseline due to therapy. 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 pCO2 (Meuret et al., 2002). Thus, a physiological measure during the VH test recovery normalized with active therapy and distinguished the active group from the waiting list group, while self-report of anxiety and symptoms for the same period did not. Among symptoms, only self-reported shortness of breath was reduced after active treatment. The improvement in physiological recovery from VH of the active treatment group was accompanied by a general and lasting improvement in panic symptomatology. The rate of improvement of recovery pCO2 at different points in therapy and at follow-up was correlated with the rate of decline in panic symptomatology and anxiety sensitivity (Meuret et al., submitted).

3. Reliability and validity of voluntary hyperventilation tests

For two of the potential roles for VH tests, diagnosis and outcome, their reliability and validity become relevant. Conclusions about these psychometric properties are likely to depend on which aspect of the tests we are considering. Response to VH includes different measures, which can be conceptualized as test items. These 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 pCO2, respiration
rate and tidal volume, heart rate, and skin conductance). 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 need to be established empirically, while the importance of different items depends on one’s theoretical perspective about anxiety.

In general, a cognitive model emphasizes self-report items since they index cognitions, a hyperventilation perspective emphasizes respiratory physiological items, and a more general psychophysiological perspective insists on both, as well as on autonomic measures for a complete picture of emotional response. Pre-VH physiological measures might seem to be an index of whether the individual tested hyperventilates habitually, but pre-test baselines are unlikely to be representative in these patients, whose anticipatory anxiety could start them to hyperventilate even before they are instructed to. Since hypocapnia and other breathing abnormalities occur during anticipatory anxiety (Alpers, Wilhelm, & Roth, 2005), pre-measures reflect an uncertain combination of how afraid an individual is of VH and the individual’s tonic anxiety levels, modulated by individual specificity and anxiety disorder specificity of the effect of anxiety on respiration.

Self-report measures during VH register how the client reacts to the sensations of hyperventilation, which is central to the catastrophic cognitions theory of panic. Respiratory sensations and the reactions to them are the essence of a putative vicious circle amplifying anxiety. According to those theories, reduction of these reactions through prolonged and repeated exposure to hyperventilation (interoceptive exposure) is an indication of therapeutic progress, although for that to be true, the reduction needs to generalize beyond the therapeutic setting. In contrast to self report, respiratory behavior during VH itself is more an index of compliance with instructions rather than of clinical change, since that behavior is prescribed by the test instructions.

Measures during the recovery period following VH can be taken to represent how well the individual copes with hyperventilation once it has occurred, one of the primary goals of BT according to the hyperventilation model. This model regards the patient’s ability to raise pCO2 levels rapidly back to normal and maintain normal breathing patterns as signs of genuine clinical improvement. Speed of recovery is likely to be registered 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 standpoint, any successful therapy should normalize previously abnormal test results, and two items repeatedly found to be abnormal in panic disorder are self-reported anxiety during VH itself (Rapee et al., 1992) and speed of recovery of pCO2 (Maddock & Carter, 1991). The latter abnormality exhibits some disorder specificity, being slowed in panic disorder but not in social phobia (Wilhelm et al., 2001).

3.1. Reliability of voluntary hyperventilation tests

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. When the VH test is prolonged or repeated, self-reported symptoms and distress tend to normalize, suggesting a lack of test–retest reliability. If the levels of pCO2 achieved during VH are kept constant, this normalization represents a growing dissociation between physiology and self-report measures. 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, but then decreased monotonically, returning to baseline levels in spite of continuation of the
VH. Maddock and Mateo-Bermudez (1990) administered two consecutive VH challenges to individuals with PD. While 50% of the patients developed symptoms of panic following the first VH test, only 25% reported symptoms after the second test 35 min later. Maddock and Carter (1991) concluded: “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. Maddock and Carter (1991) explained the low response rate to VH in the study of Gorman et al. (1988) as habituation across provocations: In that study a VH challenge was scheduled 15 min after patients had been challenged with 5% CO₂ inhalations, which could have diminished the response to VH. The subjective effects of inhaling higher than normal levels of CO₂ also tend to diminish over time (van den Hout, van der Molen, Griez, Lousberg, & Nansen, 1987).

However, that test results change when the test is repeated, rather than being a flaw, may be an indication that the test is validly reflecting a rapid reduction in fear of hyperventilation symptoms with interoceptive exposure, just as specific phobics can rapidly lose their fears when confronted with their phobic object or situation. In other words, such results may indicate real clinical improvement. This might have been the case in a study where VH challenges were the sole treatment of patients with hyperventilation syndrome (Compernolle 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, hyperventilation panic attacks disappeared with just two treatment sessions and one or two follow-up visits; the remaining patients required additional treatment for dysfunctional family interactions.

The fact that responses to VH decline when the procedure is repeated has consequences for its diagnostic use. The threshold for being identified as a member of the hyperventilator panic group may need to be set lower and lower. 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 a comparison group receiving graded in vivo exposure, the VH test was given the first time after the treatment was over. Thus, one would expect reduced HV test responsivity in the BT group at the end of treatment because of previous exposure to it, making a direct comparison of post-treatment HV measures questionable. Furthermore, exposure to feared situations in the comparison group probably entailed exposure to hyperventilation elicited by those situations, particularly for the hyperventilators, which would have resulted in diminished responses to VH over the course of treatment. Thus, the “diagnostic” VH test at the end of therapy could have underestimated the percentage of hyperventilators in the comparison group when compared to the VH test results of the BT group taken before treatment, biasing predictions of outcome based on hyperventilating status.

A decline in responses to VH when repeated is consistent with its being an outcome measure if some effective therapeutic procedure was applied between repetitions or if VH itself is therapeutic. As mentioned above, reduction may represent the therapeutic effect of interoceptive exposure and correspond to overall therapeutic improvement, but it also may fail to correspond to improvement, either because reduction with repetition and with therapy is produced by different mechanisms, or because extinction of fear does not generalize outside the VH test situation. Failure to correspond to improvement would mean that VH was invalid as an outcome measure. Conceivably, taking repetition into account might allow the validity of VH as an index of outcome to emerge. In any case, it is important for authors
to report how often VH was repeated in the various treatment groups. For example, Schmidt et al. (2000) compared CBT (including interoceptive exposure) to CBT plus BT, but although VH was part of both therapies, the authors did not say how often it was repeated in either.

3.2. Validity of voluntary hyperventilation tests

In its role as a diagnostic measure in breathing therapy studies, VH could be validated by a successful prediction of outcome. In its role as an outcome measure, concurrent validity is desirable—that an item of a VH test correlates with improvement on other measures of outcome. To a certain extent, clinicians will agree on what is improvement: when the DSM symptoms that define panic disorder diminish or disappear, the patient must be considered improved. However, theoretical considerations also play a role in how improvement is defined and assessed. From a cognitive perspective, if patients report less anxiety 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. On the other hand, from a hyperventilation perspective, cognitive therapy’s cognition-changing educational messages could have contextual demand characteristics that distort patients’ self-reports in the direction of pseudo-improvement without altering abnormal breathing. For hyperventilation theory, a good outcome would be indexed by quick recovery from hyperventilation, which is accurately indexed by change in pCO2 levels. In order to avoid that educational elements would bias self-reports, Meuret et al. (submitted) excluded 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 VH and that rationale was made. From a hyperventilation perspective, 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 challenge may leave untouched habitual respiratory dysfunction triggering attacks.

Currently the evidence for the validity of VH tests for diagnosis and measuring outcome in panic disorder is meager. As discussed above with regard to the roles of VH tests, our study did not find that initial VH test results had a predictive ability for improvement in breathing therapy. However, an important VH test measure, pCO2 during recovery from VH, had changed after treatment in the direction of normalization, which fit with the rationale of the treatment and was compatible with any of the theoretical perspectives. Confirmation and extension of such results will have to occur before VH tests can be generally accepted as valid.

4. Recommendations for standardization

One major problem in research with VH in panic disorder is that no common standard of performing the test has emerged, making comparisons between studies difficult. Standardization is needed for instrumentation, test procedures, and reporting of test methods and results. All factors known to influence the results of a VH test, particularly how often it has been repeated, should be controlled. The extent of possible standardization will depend on the actual role of VH. While standardization should be comprehensive and stringent when applied to a test of diagnosis or outcome, standardization may have to be more flexible for therapeutic applications. Standards ultimately are justified by showing that they result in a reliable and valid test or in an effective therapeutic
procedure. As of yet, VH parameters have rarely been investigated systematically, so parameter recommendations are highly tentative.

4.1. Standardization for diagnosis and outcome measurement

Any VH test worth its name must be standardized on physiological criteria of gas exchange indicating hypocapnic breathing, most importantly inferred arterial pCO\(_2\) levels (Bass & Gardner, 1985). Drawing on previous studies (Maddock & Carter, 1991; Wilhelm et al., 2001), a target end-tidal pCO\(_2\) level of 20 mm Hg seems reasonable. A relative target of 50% reduction from baseline pCO\(_2\) is an alternative, with particular appeal when patients start out with pCO\(_2\) below 30 mm Hg. Time held at the target level needs to be specified: between 2 and 6 min is customary. A post-hyperventilation recovery period may continue to yield information for as long as 8 min. Hornsveld et al. (1995) compared different durations and depths of VH in healthy controls. Their findings suggest a minimum test duration of 3 min, with end-tidal pCO\(_2\) decreasing to at least 1.9 kPa (14 mm Hg) or well below 50% of baseline in order to elicit symptoms. In our experience, 14 mm Hg would require considerable exertion for most subjects to reach, and if an absolute level is to be specified, 20 mm Hg is more easily attainable and reliably produces 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 pCO\(_2\) 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. Rates above 30 breaths/min are fatiguing and limit how long the participant will continue. In addition, very fast inspirations and expirations may be so shallow that they exceed dead space less than normal breathing, resulting paradoxically in a rise in arterial pCO\(_2\) (hypercapnia). Even worse, a measurement of end-tidal pCO\(_2\) will in this case indicate erroneously low pCO\(_2\) levels because the dead space air contains a high percentage of room air with very low CO\(_2\) concentration. Thus, instructions should require both fast, but not too fast, and deep respiration, monitored by either respiratory strain gauges or direct observation. End-tidal pCO\(_2\) should be measured with a standard capnometer, and if measured at the nostril, it is only valid if the mouth is kept tightly closed.

The outcome measures for diagnostic VH should include both self-report of anxiety and symptoms, and 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 & Medoro, 1994), should be assessed. Measures should be taken before, during, and after the VH. The speed of recovery of respiratory parameters, most importantly pCO\(_2\) (Gorman et al., 1988; Maddock & Carter, 1991), is likely to be important since pCO\(_2\) recovery is delayed in panic disorder. Autonomic measures also may be relevant, since skin conductance and heart rate also have shown delayed recovery (Wilhelm et al., 2001). The usefulness of other temporal parameters, such as speed of drop in pCO\(_2\) as minute ventilation is increased, requires further study.

Also to be controlled are overt and covert messages about the test’s purpose and what kind of experiences can be expected (e.g., whether hyperventilation can produce panic or be dangerous). 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 the character of initial information given to the patient. The setting of the test may also need to be controlled. In a recent
comparison between a VH challenge in the laboratory and the same challenge outside the laboratory during ambulatory monitoring, we observed remarkably lower intensity in certain reported symptoms, including anxiety, in the ambulatory setting (Meuret, Wilhelm, Rothkopf, & Roth, 2002).

4.2. Standardization for educational and therapeutic goals

In therapeutic settings, rigid standards for VH are undesirable. The therapist may want to reach a certain level of symptom intensity in a patient, but since patients differ in their speed of developing symptoms of hypocapnia and panic, the therapist will need to tailor VH instructions to the individual case and tell the patient to stop when the planned intensity of symptoms is reached—if possible with the help of a standardized rating scale. It is probably desirable for the patient to try breathing at about 18–22 breaths/min at about two times the patient’s usual tidal volume. This should allow the patient to reach a low pCO2 within a minute or so and maintain it for several minutes (see Wilhelm et al., 2001). When equipment for measuring physiological parameters is not available, the instructor should take extra care that patients breathe both faster and with a substantially higher tidal volume, at least twice the baseline.

All hyperventilation provocations during treatment sessions and outside them should be documented. Reports should include duration of the 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 logs for these events. The therapist also needs to assess the level of prior information patients have about hyperventilation, and patient expectations about VH. 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 descriptions of potential reactions can bias reporting and reduce the therapeutic impact of the experience.

Although in applied therapeutic settings pCO2 measurements are often perceived as uneconomical and cumbersome, the equipment will probably become cheaper and easier to use. Expanded clinical applications of capnometry (Meuret, Ritz, Dahme & Roth, 2004), including its use in emergency tracheal intubations (Cummins & Hazinski, 2000), should lower its future cost. Physiological monitoring makes sense for any application or therapy that bases its rationale on a scientific understanding of hyperventilation. As discussed above, verbal reports of hyperventilation symptoms often fail to correspond to actual physiological hyperventilation. From a hyperventilation model perspective, physiological evidence can distinguish temporary pseudo-improvement from real improvement in breathing. Subjective improvement may be reported before the habitual respiratory perturbations that may trigger hyperventilation-induced panic are corrected. In any case, regardless of therapy rationale, monitoring of respiration including pCO2 levels provides essential information to the patient and therapist about how the patient copes with real hypocapnic challenges.

5. Conclusions

Our review of BT studies in panic disorder has uncovered many uncertainties about the use of VH, some of which are due to the lack of a common reporting standard for VH procedures. 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. Applying VH as a diagnostic tool or as an outcome measure is
complicated by the reduction of self-reported responses, and possibly also of physiological responses, when VH is repeated. Test standardization depends ultimately on establishing that when VH is conducted in a specified way, certain response measures meet basic psychometric criteria of reliability and validity. Important evidence of validity is 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. We have made some tentative suggestions about plausible parameters for VH in testing and therapy, and for assessment of responses to it. Specification and recording of physiological respiratory parameters are as essential as specification and recording of self-report.

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