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Invited article

Hyperventilation syndrome: an elegant but scientifically untenable concept

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Abstract

The concept of hyperventilation and the principle of a vicious circle provide an elegant explanation for the development of a wide range of somatic and psychological symptoms, the so-called hyperventilation syndrome (HVS). The model has a high degree of credibility and has led to the development of therapeutic interventions that appeared beneficial. However, recent investigations dismiss hyperventilation as an important symptom-producing mechanism. First, the hyperventilation provocation test appears to be invalid as a diagnostic test. Second, studies using ambulant monitoring of pCO_2 demonstrate that the vast majority of real-life attacks are not attended by decreases in pCO_2. Third, the evaluation of therapy outcome studies indicate that the beneficial effect of breathing retraining is probably not mediated by reducing the tendency to hyperventilate. We conclude that a diagnosis of HVS should be avoided.

Keywords: Hyperventilation syndrome; Diagnosis; pCO_2; Psychosomatic symptoms; Panic

1. Introduction

Hyperventilation is physiologically defined in a very precise way. It is defined as ventilation in excess of metabolic requirements: the elimination of carbon dioxide occurs at a faster rate than its production in the tissues. The immediate consequence of hyperventilation is a decrease in alveolar carbon dioxide pressure (hypocapnia) and an increase of Ph in the blood (respiratory alkalosis). If sustained for some time, these physiological changes may lead to symptoms like tingling, dizziness, and cold hands and feet.

The term 'hyperventilation syndrome' (HVS) was first introduced by Kerr and colleagues [1] in 1937. They noticed the similarity between descriptions of symptoms induced by voluntary hyperventilation and symptoms of anxiety neurosis. In their study, they submitted anxiety neurosis patients to a short period of voluntary hyperventilation and demonstrated that this could reproduce many of the somatic symptoms of these patients. They considered anxiety as the initial cause of hyperventilation. One year later, Soley and Shock [2] made the connection between HVS and effort syndrome. They submitted patients with

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effort syndrome to voluntary hyperventilation and found that the symptoms could be reproduced in almost all cases. They stated that hyperventilation was the primary cause in effort syndrome and that the terms HVS and effort syndrome were in fact equal.

A differentiation within the concept of HVS was made in 1953 by Lewis [3]. He distinguished acute HVS, characterized by sudden attacks of breathlessness and tetany, from chronic HVS, characterized by persistent, often unnoticed, overbreathing resulting in a variety of symptoms, also those not very typical of acute HVS such as abdominal pains and fatigue.

Lum [4] claimed that chronic HVS was much more common than the acute form. He described HVS as a habit of faulty breathing, the symptoms of which may lead to (chronic) anxiety. This view was crucial to treatment since it meant that appropriate breathing retraining should restore the whole person and abolish the need both for psychotropic drugs and for psychotherapy.

In general, the concept of HVS has become increasingly comprehensive. The initial descriptions concerned attacks of overbreathing and tetanic symptoms. These attacks were then related to anxiety neurosis and effort syndrome. With the introduction of the term 'chronic hyperventilation', HVS was described in the absence of the typical attack-like symptoms and also in the absence of observable overbreathing. Finally, with the concept of HVS as a breathing disorder, HVS was no longer considered as necessarily caused by anxiety. Instead, the opinion gained ground that hyperventilation was the cause of a range of anxiety symptoms, especially panic and agoraphobia [5–7].

In the 1980s, the concept of hyperventilation syndrome became widely known, particularly in the Netherlands, Belgium and Britain. Several studies have indicated high frequencies of HVS: 35–83% among patients with anxiety disorder [5,6,8,9] and 5–11% among various other medical populations [10–12].

2. Doubts

Since the first descriptions, the term 'hyperventilation syndrome' has been used in many different contexts and there has been much uncertainty about its definition and diagnosis. As early as 1940, Guttmann and Jones [13], on the basis of their own research, concluded that many of the symptoms in effort syndrome, in particular the sensations of the heart, could not be explained by hyperventilation or respiratory alkalosis.

Wood [14] pointed to the similarity between anxiety neurosis and effort syndrome, but did not believe that hyperventilation was responsible for the symptoms. He stated that the symptoms in effort syndrome were invariably caused by emotional states. He proposed to use the neutral term 'DaCosta syndrome' instead of 'effort syndrome'.

In 1968, Weimann [15] emphasized that more symptoms are ascribed to HVS than are justified. He introduced the term 'HVS' in the restricted sense, including neuromuscular symptoms, cerebral symptoms, tingling and temperature sensations. Other symptoms like cardiac sensations and anxiety were indeed mentioned frequently by HVS patients, but did not belong to the HVS in the restricted sense.

Dent, Yates and Higgenbottam [16] under the expressive title "Does the hyperventilation syndrome exist?" emphasized the need for a careful assessment to exclude underlying diseases. They found that almost half of their patients—patients with a history compatible with hyperventilation syndrome—had treatable mild asthma or hyperthyroidism.

At the 8th Annual Symposium on Respiratory Psychophysiology in 1990, Gardner proposed to refrain from using the term 'hyperventilation syndrome' because of a lack of consensus regarding cause, diagnosis, and classification. He preferred the more descriptive term 'chronic hyperventilation of unknown cause' [17].

During recent years, critical studies on HVS have steadily increased. Our own series of investigations highly contributed to this development [18]. In the present review we will summarize the main findings of these studies. Successively, we will present two validation studies on the hyperventilation provocation test [19,20], two studies using measurement of pCO_2 during spontaneous symptom attacks [20,21] and one evaluation study on breathing therapy [22]. In subsequent sections, the conclusions will be summarized, some ancillary findings will be presented and the practical implications will be dealt with.

3. The hyperventilation provocation test

The concept of HVS assumes that no organic diseases are underlying the symptoms, such as cardiac, pulmonary, or neurological diseases. Organic causes of hyperventilation must be excluded as well [23]. Symptoms may not be used as a basis for diagnosis since they are non-specific. Similarly, hyperventilation may not be inferred from the breathing behaviour. The patient may be hypocapnic without visible overbreathing, and, on the other hand, panting may be obvious without concomitant hypocapnia.

HVS is generally diagnosed on the basis of a hyperventilation provocation test (HVPT), which requires voluntarily hyperventilation for several minutes. The test is considered positive if the induced symptoms are similar to those experienced in daily life [19,23]. Reproducibility of daily-life symptoms is considered to be the cornerstone in the diagnosis of HVS, but the importance of additional physiological criteria has been emphasized, especially lowered arterial or end-tidal resting pCO_2 values [24] and a delayed recovery of pCO_2 after voluntary hyperventilation [25].

The major problem with the HVPT is that this test does not distinguish between symptoms produced by hypocapnia and those produced by other factors such as the mechanical discomfort of rapid deep breathing, or the stressfulness of the procedure. This might imply that exposure of patients to other types of challenges can reproduce a similar symptom pattern.

The Swedish cardiologist, Roll [26], compared the HVPT and a stressful mental load task in a group of patients attending an emergency care unit because of chest pain without obvious organic cause. During the HVPT, 44% of the patients said they recognized the symptoms, but a similar percentage (38%) recognized the symptoms during the stressful mental load task, although no hyperventilation occurred during this task. We replicated this study in a group of patients with divergent symptoms suggestive of HVS [19] and obtained highly similar findings. These results suggest that symptom recognition during the HVPT is not specifically related to the hypocapnic state.

In a subsequent study we used a double-blind placebo-controlled design to validate the HVPT
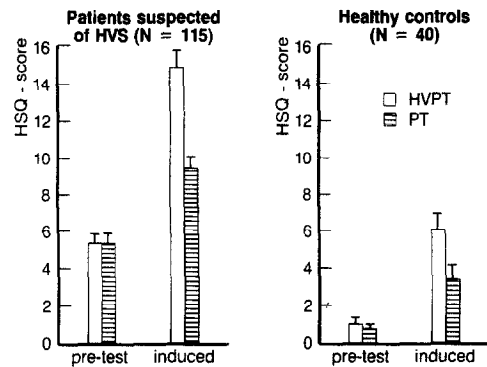

Fig. 1. Means of the Hyperventilation Symptom Questionnaire (HSQ) for number of pretest symptoms and induced symptoms during the hyperventilation provocation test (HVPT) and placebo test (PT). Bars indicate standard error of the mean.

[20,27]. The placebo-HVPT consisted of isocapnic overbreathing: subjects breathed as if they were hyperventilating but the CO_2 drop was prevented by adding CO_2 to the inspired air. The sample consisted of 115 HVS suspected patients who were referred to a Lung Function Laboratory of a general hospital and a group of healthy controls. Patients reported significantly more symptoms than controls, both at pretest, during the HVPT, and during the placebo-HVPT (see Fig. 1). In Fig. 1 it can also be seen that the HVPT brought about more symptoms than the placebo test [1]. However, the placebo test, too, endorsed a considerable number of symptoms; about 2/3 of the symptoms that were reported during the standard hyperventilation test also occurred during the placebo test. In this respect, patients and controls did not differ.

Symptom recognition during the HVPT (positive diagnosis HVS) was reported by 74% patients. Of that subset, 2/3 were also positive on the placebo test (false positive), and 1/3 were negative on the placebo test (true positive). We investigated whether these 'true positive' patients would fit the hyperventilation model. We predicted that these patients would suffer from more typical hyperventilation symptoms

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[1] Compared to the placebo-HVPT, the HVPT induced significantly more neuromuscular symptoms, cerebral symptoms, paresthesias and temperature sensations. Respiratory symptoms and cardiac symptoms were reported almost as frequently during the HVPT as during the placebo test (see Ref. [27] for details).

(neuromuscular symptoms, cerebral symptoms, paresthesias and temperature sensations), and would meet physiological HVS criteria more frequently (slow recovery of $PetCO_2$ and low $PetCO_2$ at rest). However, true-positive and false-positive patients did not differ in any of the symptom variables or on physiological variables. In other words, the distinction between true-positives and false-positives did not seem meaningful.

The above results clearly demonstrate that symptom recognition during the HVPT is invalid as a diagnostic test for HVS. Even the combination of an HVPT and a control test yields invalid diagnoses. In the same study, we found that physiological HVS criteria were also not helpful [20]. Delayed recovery of end-tidal pCO_2 after hyperventilation appeared not specific for patients compared to controls. This finding accords with those of many other investigators, who were likewise unable to replicate the original findings of Hardonk and Beumer [25]. A resting end-tidal pCO_2 of less than 4 kPa, a presumed indicator of HVS [24], appeared not to be diagnostically specific, although mean end-tidal pCO_2 was somewhat higher in healthy controls than in patients.

Symptom recognition during the HVPT is the most widely used and accepted criterion for HVS. Almost equally widespread [28] is the criterion of a delayed recovery after voluntary hyperventilation. They both have face validity. It is often very convincing when a patient says that the HVPT-induced symptoms are the same as his/her usual symptoms. Similarly, when a patient is unable to stop over-breathing after the HVPT (delayed recovery), this resembles descriptions of uncontrollable breathing that is experienced during spontaneously developing attacks. But, plausibility aside, the test is not valid. Note that this removes the pillars on which the hyperventilation theory rests: the procedure to diagnose a patient as hyperventilant seems to be invalid.

4. Ambulant pCO_2 monitoring in HVS-suspected patients

While these findings are very serious to the hyperventilation theory, it does not rule out that, in real life, patients do hyperventilate. The only way to test this would be to assess CO_2 levels during sponta-

neous symptom attacks. Recent technological advances using transcutaneous measurement of arterial pCO_2 do allow for this assessment [29].

We have applied this method in two studies. The first study was performed in an anxiety disorder clinic with 28 outpatients who met the DSM-III-R diagnosis of panic disorder with agoraphobia [21]; the second study was performed in a general hospital with 30 HVS-suspected patients who were either true- or false-positive on the HVPT (see Section 3) [20]. All subjects wore the ambulatory monitor on 2 separate days. They were instructed to press a marker button whenever they felt an attack or substantial worsening of symptoms.

In both studies it was found that the vast majority of attacks were not attended by any drops in pCO_2. In the study with panic disorder patients, 24 panic attacks were registered. A decrease in pCO_2 was observed during only one of these attacks, and even during this particular attack the degree of hyperventilation was not impressive. In the second study, with positively diagnosed HVS patients, we registered 22 attacks. In only 7 of these 22 attacks did $PtcCO_2$ actually decrease. These decreases were mild and apparently followed the onset of the attack, rather than preceding it. In this respect, true-positives and false-positive patients did not differ.

5. Therapy outcome studies

Several intervention methods have been proposed as treatments for HVS. Breathing retraining, logically derived from the HVS theory, is often a major component. Most of these therapies appear to be effective, both for HVS patients and for panic disorder patients. This would suggest that alteration in ventilatory parameters is central to symptom formation and alleviation.

In comparing all available outcome studies we found the specificity of breathing therapy to be questionable [22]. In one study, for example, 7 types of treatment for HVS were given [30]. All types resulted in significant decreases in the patients' pathology compared to a waiting list control group, but there were no differences between therapies that did and that did not include breathing retraining.

The conclusion is that the effects of breathing retraining are probably not mediated by reducing the

tendency to hyperventilate. It is highly probable that many symptoms are related to a tense or inefficient breathing pattern rather than to overbreathing *per se*. Breathing therapy may improve this breathing pattern and alleviate the associated symptoms. Aspecific factors such as reassurance, relaxation and increased sense of control may contribute as well. In any case, the beneficial effects of breathing retraining may not be considered as validating the HVS model.

6. The validity of the hyperventilation syndrome

The estimated prevalence of HVS was based on symptom recognition during an HVPT. Since we now know that the HVPT is not valid, we cannot avoid the conclusion that many patients have been misdiagnosed in the past. Incidence rates have to be re-examined.

The equipment for ambulant monitoring of pCO_2 has the potential of a gold standard, since it enables determining whether HVS-suspected patients really hyperventilate during spontaneous symptom episodes. On the other hand, the concurrence of symptoms and hyperventilation does not necessarily imply that hyperventilation *causes* the symptoms. Hyperventilation may also be a simultaneously occurring phenomenon (epiphenomenon) together with the presence of (certain kinds of) somatic or psychological symptoms. We found that hyperventilation occurred in only a few attacks and, even in these attacks, pCO_2 seemed to decrease following the onset of the attacks. In none of our patients could it be demonstrated that hyperventilation significantly contributed to the onset or severity of the symptoms.

It must be concluded that patients hyperventilate much less frequently than was previously assumed. When they do hyperventilate, it seems a consequence or epiphenomenon of the attack rather than a contributor to the onset or severity of it. This implies that the term HVS has become untenable.

The above conclusions are probably not valid for a small subgroup of patients with chronic hyperventilation. Neither the ambulatory $PtcCO_2$ measurement technique nor single observations of end-tidal pCO_2 adequately address the issue of chronic hyperventilation. It seems more appropriate to determine base excess (BE) in the blood, a marker of metabolically compensated respiratory alkalosis [31,32]. Clinically relevant decreases in BE (less than −2 mmol/l) were found in 14% [31], 9% [33] and 5% [34] of HVS-suspected patients. More research seems necessary in this subgroup of patients.

7. Psychological influences on symptom reporting

In our studies we found a close relationship between somatic symptom reporting and psychological variables, such as anxiety, agoraphobia, depression, hypochondriac attitudes and fear of physical symptoms. Thus, the more anxious subjects were prior to the tests, and the more anxious, hypochondriac and depressive they were in general, the more symptoms were induced during the tests [27,35,36].

The positive relationship between the report of symptoms and various psychological measures was not characteristic for the patient samples but was present in healthy controls as well [27,35]. This is in line with the idea that somatic symptoms are not only associated with psychological factors for a psychiatric or neurotic minority, but for all people [37,38]. We also found that the more 'hyperventilation symptoms' a person experiences, the more 'non-hyperventilation symptoms' (e.g., low back pain, itching, sore throat) were experienced as well. This suggests the significance of a general tendency to report somatic symptoms in these patients [39].

Rejection of hyperventilation as an important symptom-producing mechanism does not mean that all aspects of the HVS model are invalid. HVS is usually described as a vicious circle process in which physical, cognitive and behavioural factors interact. Hyperventilation may play a role, but other bodily changes may as well, such as physiological arousal, physical exercise, sleep disturbance, drug abuse or muscle tension. An inefficient breathing pattern, not necessarily associated with pCO_2 changes, may contribute to symptom formation in a subset of patients.

An important factor in the maintenance of the symptoms seems to be the cognitions and behaviours of the patient. These may prevent an adequate approach to the problem. Examples of the potentially problematic assumptions that patients may have about the nature of their symptoms are "bodily changes are usually a sign of serious disease", "every symp-

tom has to have an identifiable physical cause'', or "there's heart trouble in the family". As a result, such patients may selectively notice and remember information which is consistent with their beliefs about their problems. Further bodily sensations and other illness-relevant information are then more likely to be noticed as a consequence of increased vigilance arising from anxiety. If symptoms are catastrophically interpreted, this may lead to panic (if the feared catastrophe is immediate, e.g., "I am having a heart attack right now") or to serious health concern and hypochondriasis (e.g., "The pain in my stomach means I have undetected cancer"). Avoidance behaviour, such as 'reassurance seeking' and 'checking bodily status' may be an important factor in maintaining health anxiety [40]. Symptoms may be conceptualized as 'mini-catastrophes'; they do not directly lead to full-blown panic or hypochondriasis, but may nevertheless be regarded as symptomatic of a disease.

8. HVS: an attractive diagnosis?

To many patients a diagnosis of HVS is a positive diagnosis, preferable to 'nothing wrong with your heart', 'no brain tumour', or 'nothing serious'. It provides an acceptable somatic explanation for the symptoms while other relevant factors are also being recognized (life-events, daily hassles, interpretative biases or other psychological factors). For the same reasons, HVS is an attractive diagnosis for doctors as well. Doctors often feel empty-handed if no disease diagnosis can be given [41]. HVS is an attractive alternative with the added advantage that it is less threatening than a 'pure' psychosocial explanation or a psychiatric diagnosis, such as panic, phobia, hypochondriasis or somatization. There seems to be no single alternative with the same advantages to replace HVS.

On the other hand, the concept of HVS also has its drawbacks. The excessive use and misuse of the term 'HVS' has given it the negative loading of a fashionable disease that is not to be taken seriously. The concept of HVS has become increasingly comprehensive and has more or less become a reservoir for all kinds of patients with medically unexplained symptoms. The diagnosis is sometimes made to reas-

sure patients without thorough physical examination [42] or without enquiring the causes of the presumed hyperventilation. Labelling symptoms as hyperventilation symptoms suggests that the causes are known and that breathing therapy (alone or in combination) will be beneficial. Moreover, some patients may not feel reassured by a diagnosis of HVS. The idea that symptoms are due to some unnoticed or imperceptible overbreathing may strengthen the feeling of lack of control over the symptoms.

We believe that a diagnosis of HVS should be avoided. Firstly, for scientific reasons, but also because of the above-mentioned disadvantages of the term 'HVS'. However, farewell to the HVS will not change the number of patients that present with physical symptoms for which no medical explanation can be found.

9. Practical implications

In recent years, panic disorder has become one of the most studied syndromes in psychopathology. This research has yielded much knowledge relevant to the understanding and treatment of a subgroup of what used to be HVS patients [43]. Breathing retraining has some beneficial effects, but the effects tend not to be impressive and can easily be attributed to non-specific effects. For panic disorder patients, cognitive behaviour therapy seems to offer a better perspective. Recent studies suggest that this kind of therapy can eliminate attacks in 75–90% of the patients.

In medical practice, most patients have no diagnosable psychiatric disorder. Careful assessment and reassurance by the physician may be sufficient, but sometimes reassurance has no or an adverse effect and specialized treatment seems necessary. Relatively little is known about how patients might best be reassured: that is, without being tempted to use 'semi-medical' diagnoses like 'hyperventilation'. Similarly, it is necessary to know how to motivate patients who are reluctant to visit a psychologist or psychiatrist.

Recently, cognitive behavioural therapy was offered to a group of patients with persistent medically unexplained symptoms in a general medical outpatient clinic. This therapy appeared more effective

than optimized medical care (the quality of medical care was enhanced through provision of basic psychiatric training for the physicians) [44]. Most patients were willing to accept the cognitive behavioural therapy. The fact that the study was introduced by the attending physician and that the treatment sessions took place in the general medical outpatient clinic itself was considered to be important in preventing patients from feeling that referral for psychological assessment represented dismissal by the physician.

Probably the most direct result of our studies is that the HVPT as a diagnostic test can best be abolished. In the Slotervaart Hospital, where the presented research has been conducted, the HVPT has been replaced by an outpatient department for patients with medically unexplained symptoms. At the request of medical specialists and general practitioners a psychodiagnostic assessment is performed, including advice for further referral, if desired. Besides diagnosis, there are some modest therapeutic aims, such as providing some insight into the relationship between the symptoms and psychosocial factors, reassurance with respect to their fear of a serious disease or to disaffirm the belief that it is now 'all psychic' and 'between the ears'.

10. Final remark

The presented research provided evidence on "what it is not". In this sense, the hyperventilation syndrome may join its predecessors, such as irritable heart and neuro-circulatory asthenia, as a premature aetiological explanation for somatic symptoms. Although other biological and psychophysiological factors should certainly be further explored, it seems unlikely that future research will identify a single system or single dysfunction that gives rise to the wide variety of unexplained somatic symptoms previously associated with HVS.

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