Is chronic fatigue syndrome synonymous with effort syndrome?

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Keywords: chronic fatigue syndrome; effort syndrome; hyperventilation; capnography; performance-arousal curve

Summary
Chronic fatigue syndrome (CFS), including myalgic encephalomyelitis (ME) and postviral syndrome (PVS), is a term used today to describe a condition of incapacity for making and sustaining effort, associated with a wide range of symptoms. None of the reviews of CFS has provided a proper consideration of the effort syndrome caused by chronic habitual hyperventilation. In 100 consecutive patients, whose CFS had been attributed to ME or PVS, the time course of their illness and the respiratory psychophysiological studies were characteristic of chronic habitual hyperventilation in 93. It is suggested that the labels 'CFS', 'ME' or 'PVS' should be withheld until chronic habitual hyperventilation - for which conventional rehabilitation is available - has been definitively excluded.

Introduction
Chronic fatigue syndrome (CFS), including myalgic encephalomyelitis (ME) and postviral syndrome (PVS), is a name given to a condition of incapacity for making and sustaining effort, associated with a wide range of symptoms[1-8]. The disability and the symptoms are similar to those found in chronic habitual hyperventilation or effort syndrome[9-15]. The purpose of this paper is to report a study of the prevalence of chronic hyperventilation in 100 consecutive patients previously given the diagnosis of CFS and 40 asymptomatic control subjects. During the study, it emerged that the time relationships between the onset of symptoms and the occurrence of real or purported viral infection were significant. These were also recorded and the results are presented.

Subjects
One hundred consecutive patients (34 male, 66 female, with a mean age of 36.5 years ±11; range 15-78 years) diagnosed elsewhere as having CFS and 40 asymptomatic volunteers (14 males, 26 females with a mean age of 40.2 years ±14; range 19-72 years) recruited from hospital staff, were studied.

Methods
The patients' case histories were taken and a clinical examination made to exclude those with hitherto undiagnosed organic disease. In all subjects, peak flow readings were obtained to exclude obstructive airways disease. Assessments of loss of performance, time course of illness and respiratory psychophysiological responses were made.

Assessment of loss of performance
Subjects stated as a percentage their perception of the loss of energy, stamina, concentration and memory that had taken place since they were last capable of making and sustaining effort in the way they considered normal for them.

Time course of illness
The histories of the first patients suggested that the real or purported illness was not the start of the disorder, but a marker of deterioration after a period of infirmity. Accordingly, we paid close attention to time relationships in the last 65 patients. We noted when they last considered themselves to be capable of normal performance, the period between that time and the appearance of the real or purported viral illness and the period between that event and the date of examination in this department.

Respiratory psychophysiological assessments
These were made with the subjects comfortably seated in a chair. End-tidal carbon dioxide levels (Pet CO_2) were recorded by means of an IL 200 infrared mass spectrophotometer, a capnograph, analysing the air drawn continuously through a fine bore plastic tube held within the dominant nostril by a lightweight headband.

The capnograph was calibrated by means of a Corning calibration cylinder (5% CO_2, 12% O_2, 83% N_2) with a daily correction for barometric pressure to permit Pet CO_2 to be measured on a mmHg scale. Pet CO_2 recordings were taken with a 2 channel Devices recorder. Tracings at a paper speed of 25 mm/s were examined to ensure that alveolar plateaux developed in each case. Under these conditions the differences between Pet CO_2 and arterial CO_2 tension (Pa CO_2) are minimal[16]. Thereafter, a paper speed of 0.1 mm/s was used for the testing which had four parts:

(1) The resting Pet CO_2 was noted, and a value of 29 mmHg or less was deemed positive for hypocapnia.

(2) A forced hyperventilation provocation test (FHPT) was performed to assess the individual's tendency to continue to overbreathe after stimulation by breathing deeply and rapidly for 3 min and reducing the Pet CO_2 to 20 mmHg or less[17]. Three minutes after cessation of overbreathing the Pet CO_2 was noted and expressed as a percentage of the resting Pet CO_2 level. In accordance with Hardonk and Beumer, values below 66% were considered positive.

(3) Between 3 and 4 min from the end of the FHPT, the subjects were asked to close their eyes for the 'think test'[18].

The lowest point (nadir) of Pet CO_2 reached in the 'think test' was noted and expressed as a percentage of the resting Pet CO_2. The 'think test' was considered positive if the Pet CO_2 fell by 10 mmHg or more

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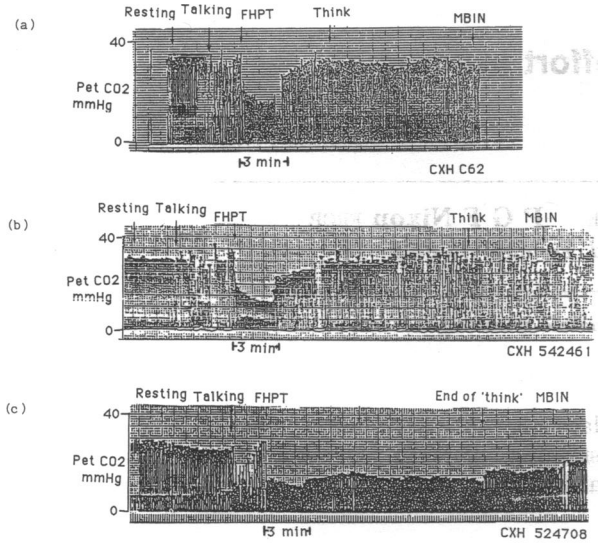

Figure 1. Capnograms - these display continuous reading of the partial pressure of carbon dioxide in the exhaled air. The upper level describes the end-tidal value (Pet CO_2) (measured here in mmHg). The sequence of tests is described in the text, ie the resting level; the forced hyperventilation provocation test (FHPT)[17], the nadir of the response to recall of personally-relevant stressors ('think test')[18] and the Pet CO_2 level felt to be normal after the tests described, marked 'MBIN', standing for 'my breathing is normal'[19] (a) Normal capnogram; (b) pattern of hyperventilation showing arrhythmic breathing[20]; (c) pattern of hyperventilation showing a fall in Pet CO_2 and failure of Pet CO_2 to rise after FHPT and during 'think test'

from a starting level of 30 mmHg or above, or fell 6 mmHg if the starting level was 29 mmHg or below[18].

(4) At the end of the 'think test', each subject was asked to open his eyes, to relax, and to signal by raising a hand as soon as the breathing felt 'normal'. The Pet CO_2 at this level was noted and expressed as a percentage of the resting Pet CO_2[19]. This 'perception' test was arbitrarily considered positive if the Pet CO_2 at the 'normal' signal was $\leqslant 80\%$ of the resting level. The testing of the control group followed the procedure adopted for the patients. After the FHPT they were asked to think about personally-relevant mental stressors and emotionally-charged experiences associated with anger, despair, fear and happiness. An example of a normal capnogram is shown in Figure 1(a).

The capnograph not only provides measurements of Pet CO_2 but also allows patterns of inappropriate breathing to be identified. These include an arrhythmic pattern of breathing, with marked irregularities of Pet CO_2, as described by Evans and Lum[20] and shown in Figure 1(b); and the Pet CO_2 level falling during the control period where a steady state would be expected or failing to rise where an upward course would be appropriate, as for example, after the challenges of the FHPT or the 'think test' (Figure 1(c)).

Statistical analysis

't'-tests were used to compare subjects' and controls' scores on both the percentage scales and the respiratory psychophysiological assessments.

Results

Clinical assessments

The findings were consistent with the diagnosis of chronic habitual hyperventilation in every case.

Assessment of loss of performance

There was a significant reduction of performance (in the categories of energy, stamina, memory and concentration, mentioned above), to a mean of 40% of the self-perceived 'normal' trait for that individual. (This value is the arithmetic mean of the values shown in Table 1). In the control group, the reduction was to a mean of 77%.

Time course of illness

Data was available on this point for 65 of the patients and the results are presented in Table 1 and Figure 2. The mean period between the supposed or genuine viral infection considered by the patient to be the trigger of his/her illness and the consultation with us was 3.5 years. However, the mean period between the point when the patient last considered him/her self to be capable of 100% normal performance and the consultation was 5.8 years. It can thus be seen that a mean period of 2.3 years of loss of performance and non-specific ill health consistent with chronic hyperventilation pre-dated the supposed trigger.

Discussion

The symptoms and signs presented by these patients, made effort syndrome (hyperventilation due to anxiety and effort) a reasonable diagnosis for consideration, and we agree with Rice[13], Lum[14] and Magarian[15] that many clinicians are reluctant to

Table 1. Loss of performance self-rated by subjects and expressed as a percentage of their norm, and, for patients, the time course of their illness

	n	*Energy (%)*	*Stamina (%)*	*Concentration (%)*	*Memory (%)*	n	*Time from 100% to consultation (years) (a)*	*Time from purported illness to consultation (Years) (b)*	*(a)−(b)*
Patients	100					65			
Mean±SD		30.9±18.1	33.8±21.5	46.0±23.2	50.1±25.2		5.8±5.7	3.5±4.2	2.3±2.6
Range		0-75	0-80	5-99	5-99		0.6-27	0.2-25	0-15
Controls	40								
Mean±SD		74.8±8.4	77.5±11.2	79.8±10.1	74.9±10.6		—	—	—
Range		60-90	50-90	55-95	60-95				

$P<0.001$

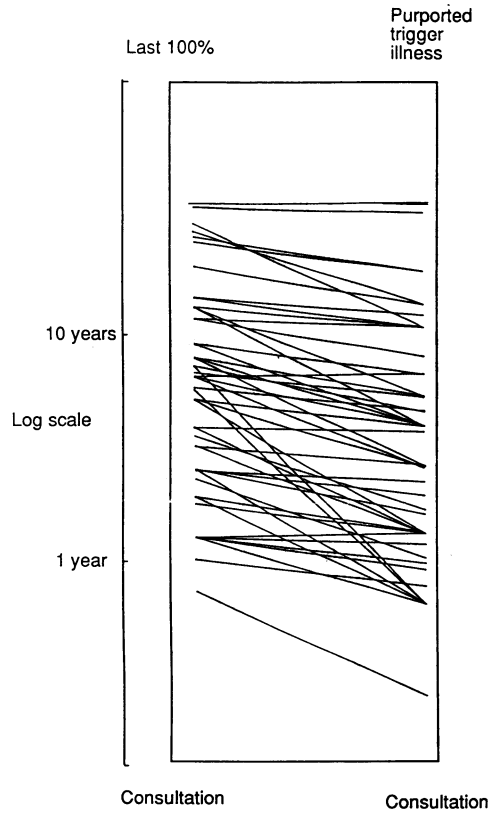

Figure 2. Length of time from when last self-rated 100% until consultation and length of time from purported trigger illness until consultation

acknowledge the existence today of a condition which formerly was considered to be common.

It was interesting when taking the histories to note that in the earlier phases the patients were bitterly resentful at failure of diagnosis. In the later stages the anger and frustration were replaced by a flat acceptance of disability as the subjects 'gave in' or 'gave up' the struggle to be well, and adapted to infirmity.

These two phases resemble Sargant's[21] findings in wartime exhaustion: an initial, more superficial period characterized by anxiety, panic states and phobic disorders, neurological complaints, cardiovascular deconditioning, and cardiovascular instability with chest pains, palpitations and breathlessness. This was followed by a deeper 'vegetative' phase where recovery appeared to be inhibited. Sargant had no means of measuring Pet CO_2, but Lum[22] was able to describe the physiological basis for these phases in the syndrome of chronic habitual hyperventilation. We commonly meet these phases in cardiac rehabilitation today, particularly after the treatment of myocardial infarction in hospital or open-heart surgery[23] and believe that the CFS diagnosis is a label erroneously put upon the deeper phases of effort syndrome.

There are a number of reasons for impairment of muscular function in effort syndrome. These include depletion of the alkali reserves[9]; salt and water retention[24]; the cells having a reduced potassium[25] and magnesium content[26], and increased calcium ionisation[27] and autonomic deconditioning[28]. Nowadays, we attribute Sargant's inhibition of recovery to depletion of the body's buffer base reserves, and to the consequences of profound sleep disturbances that follow depletion of the alkali reserves[29].

The study of the controls supports the view that hyperventilation in itself cannot be regarded as a

Table 2. Respiratory psychophysiological assessments (in mmHg)

	n	*Resting Pet CO_2*	*3 min post FHPT*	*Nadir of 'think test'*	*MBIN*
Patients	100				
Mean±SD		35.0±4.6	30.4±6.1	25.1±5.3	29.2±5.8
Range		24-45	17-44	12-38	15-40
Controls	40				
Mean±SD		35.2±4.6	30.5±6.8	29.1±6.1	33.6±5.1
Range		25-45	15-44	15-40	22-42

$P<0.001$

pathological process. Many individuals can and do overbreathe in the course of their daily lives and it is an appropriate response to conditions causing vigilance and emotional arousal[30,31]. It is probable that the people who become ill with the physiological consequences of hyperventilation are those who overbreathe more vigorously and for longer periods of time, and respond to smaller stimuli when they are overtired and anxious. Failure of professional acknowledgment of their predicament and support in it increases anxiety and therefore sympatho-adrenal arousal[14]. This compels further hyperventilation[30] which, in turn, generates more sympatho-adrenal activity and anxiety, the vicious circle described by Lewis[32]. One of the first therapeutic aims is to break this circle.

There are a number of reasons for failure of diagnosis of chronic habitual hyperventilation. Amongst these are the facts that the respiratory pattern is generally unobtrusive[33], and most patients fail to report their overbreathing because their perception of hypocapnia is deficient[19,32]. The unfortunate assumption on the part of action groups that hyperventilation is synonymous with hysterical overbreathing has led to hyperventilation being taken as an insulting suggestion that the illness is 'all in the mind'.

In an attempt to dismiss the aetiological role of hyperventilation, it is claimed by some that the breathing disturbance is the consequence of a chronic illness induced by viral infection. However, the observation of more than two years of health impairment consistent with hyperventilation prior to the date of the viral infection suggests that the latter is probably opportunistic. In cases without an actual

Table 3. Numbers of patients and controls with positive evidence of hyperventilation

Test	*Positive in controls (n=40)*	*Positive in patients (n=100)*
(a) Resting Pet CO_2	4 (10%)	13
(b) 3 min post FHPT	3 (7.5%)	9
(c) 'Think test'	8 (20%)	53
(d) Breathing signalled 'normal' (<80% of a)	10 (25%)	39
(e) 1 of (a) to (d) positive	19 (47.5%)	78
(f) (e) plus capnographic patterns of hyperventilation	22 (55%)	93

viral infection, the onset of malaise and muscular pains is consistent with simple deepening of the hyperventilation disorder.

The physiological disorders of effort syndrome rarely feature in undergraduate education and sponsored postgraduate meetings, and are therefore unfamiliar to many doctors. When the diagnosis does not come to mind there are many tempting alternatives such as anxiety syndrome, or phobic disorder, included in the American Psychiatric Association's catalogue DSM III R[34], in addition to the CFS label. Furthermore, it appears that many doctors are unfamiliar with the psychophysiological and behavioural disorders that develop when healthy people are driven beyond the boundaries of physiological tolerance, and they too easily accept viral infections as causative rather than as opportunistic. It has long been recognized that hyperventilation-related illness can appear after or be aggravated by injury or infection[14].

A further reason for lack of diagnosis may be the absence of readily available testing. Capnography is not widely available, but that did not prevent Sir Thomas Lewis[9] from recognizing the loss of buffer base and providing an effective therapeutic regimen in World War I. We suggest that it is reasonable to use a sleeping-resting regimen as a therapeutic test and adopt a conventional course of rehabilitation[23,31] before consigning the patient to a fashionable therapeutic cul de sac.

Claude Bernard[35], George Engel[36] and Rene Dubos[37] have viewed healthy function as the biological reward for living within the boundaries of physiological tolerance. Effort syndrome, hyperventilation due to anxiety and effort, may be the natural penalty for violation.

Acknowledgments: The authors thank their colleagues in Occupational Therapy, Miss S Wilson, Miss K Mosely, and Miss S Walls for their help, and the Rayne Foundation, Smith's Charity, and United Biscuits for their generous support.

References

1 Valdini AF. Fatigue of unknown aetiology. *Fam Pract* 1985;**2**:1
2 Lloyd AR, Wakefield D, Boughton C, Dwyer J. What is myalgic encephalomyelitis? *Lancet* 1988;i:1286-7
3 Holmes GP, Kaplan JE, Gantz NM, *et al.* Chronic fatigue syndrome: a working case definition. *Ann Intern Med* 1988;**108**:387-9
4 Swartz MN. The chronic fatigue syndrome - one entity or many? *New Engl J Med* 1988;**319**:1726-8
5 Murdoch JC. The myalgic encephalomyelitis syndrome. *N Z J Med* 1989;ii:372-3
6 Wessely S, Powell R. Fatigue syndromes: a comparison of chronic postviral fatigue with neuromuscular and affective disorders. *J Neurol Neurosurg* 1989;**52**:940-8
7 Bowman SJ, Brostoff J, Newman S, Mowbray JF. Postviral syndrome - how can a diagnosis be made? A study of patients undergoing a Monospot test. *J R Soc Med* 1989;**82**:712-16
8 Wessely S. Chronic fatigue and myalgia syndrome. In: Sartorius N, Goldberg G, de Girolamo G, *et al.* eds. *Psychological disorders in general medical settings.* Toronto: Hogrefe and Huber, 1990:82-97
9 Lewis T, Cotton C, Barcroft J, Milroy TR, Dufton D, Parsons TR. Breathlessness in soldiers suffering from irritable heart *BMJ* 1916;ii:517-19
10 Lewis T. *Diseases of the heart.* London: MacMillan, 1933:158-9
11 Kerr WJ, Dalton JW, Gliebe PA. Some physical phenomena associated with the anxiety states and their relation to hyperventilation. *Ann Intern Med* 1937; **11**:962-92
12 Soley MH, Shock NW. The aetiology of effort syndrome. *Am J Med Sci* 1938;**196**:840-51
13 Rice RL. Symptom patterns of the hyperventilation syndrome. *Am J Med Sci* 1950;**8**:691-700
14 Lum LC. The syndrome of chronic hyperventilation. In: Hill OW, ed. *Modern trends in psychosomatic medicine. 3.* London: Butterworth, 1976:196-230
15 Magarian GJ. Hyperventilation syndromes: infrequently recognised common expressions of anxiety and stress. *Medicine* 1982;**61**:219-36
16 Collier CR, Affelt JE, Farr AF. Continuous rapid infrared CO2 analysis. *J Lab Clin Med* 1955;**45**:526-39
17 Hardonk JH, Beumer HM. Hyperventilation syndrome. In: Vinken PJ, Bruyn GW, eds. *Handbook of clinical neurology,* vol. 38. Amsterdam: North Holland, 1979:309-60
18 Nixon PGF, Freeman LJ. The 'think test': a further technique to elicit hyperventilation. *J R Soc Med* 1988;**81**:277-9
19 King JC, Rosen SD, Nixon PGF. Failure of perception of hypocapnia after diagnostic testing in cardiovascular patients with hyperventilation-related disorders. *J R Soc Med* 1990;**83**:765-7
20 Evans DW, Lum LC. Hyperventilation as a cause of chest pain mimicking angina. *Practical Cardiology* 1981;**7**:131-9
21 Sargant W. *Battle for the mind.* London: Heinemann, 1957:22-36
22 Lum LC. Hyperventilation and anxiety state. *J R Soc Med* 1981;**74**:1-4
23 King JC, Nixon PGF. A system of cardiac rehabilitation: psychophysiological basis and practice. *Br J Occup Ther* 1988;**51**:376-84
24 Theorell T, Lond E, Froberg J, Karlsson CG, Levi L. A longitudinal study of 21 subjects with coronary heart disease: Life changes, catecholamine excretion and related biochemical reactions. *Psychosom Med* 1972; **34**:505-16
25 Pearson MG, Quadiri Mr, Fina R. Hypokalaemia with chronic hyperventilation syndrome. *Br J Clin Pract* 1986;**40**:28-9
26 Ebel H, Gunther T. Role of magnesium in cardiac disease. *J Clin Chem Clin Biochem* 1983;**21**:249-65
27 Yasue H, Ornote S, Takizawa A, Nagao M, Nosakak, Nakajima H. Alkalosis-induced coronary vasoconstriction. Effects of calcium, diltiazem, nitroglycerine and propranolol. *Am Heart J* 1981;**102**:206-10
28 Mantisaari M. Haemodynamic reactions to circulatory stress tests in patients with neurocirculatory dystonia. *Scand J Clin Lab Invest* 1984;**44**:Suppl 170
29 Ley R. Panic attacks during sleep: a hyperventilation-probability model. *J Behav Ther Exp Psychiatry* 1988;**19**:181-92
30 Groen JJ. The measurement of emotion and arousal in the clinical physiological laboratory and in clinical practice. In: Levi L, ed. *Emotions: their parameters and measurement.* New York: Raven Press, 1975:727-46
31 King JC. Hyperventilation: a therapist's point of view: discussion paper. *J R Soc Med* 1988;**81**:532-6
32 Lewis Bl. The hyperventilation syndrome. *Cal Med* 1959;**91**:121-6
33 Okel BB, Hurst JW. Prolonged hyperventilation in man: associated electrolyte changes and subjective symptoms. *Arch Intern Med* 1961;**108**:751-62
34 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders.* Washington: American Psychiatric Association, 1987
35 Bernard C. In: Bayliss CE, ed. *Principles of general physiology.* London: Longman, 1960:721-2
36 Engel GL. The clinical application of the biopsychosocial model. *Am J Psychiatry* 1980;**137**:535-44
37 Dubos R. *Man adapting,* New Haven: Yale University Press, 1980

(Accepted 16 July 1990)