Journal of Neurology, Neurosurgery, and Psychiatry 1989;52:940–948

Fatigue syndromes: a comparison of chronic "postviral" fatigue with neuromuscular and affective disorders

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SUMMARY Patients (n = 47) presenting to a neurological centre with unexplained chronic "postviral" fatigue (CFS) were studied prospectively. Controls were patients with peripheral fatiguing neuromuscular diseases and inpatients with major depression in a psychiatric hospital. Seventy-two percent of the CFS patients were cases of psychiatric disorder, using criteria that excluded fatigue as a symptom, compared with 36% of the neuromuscular group. There was no difference in subjective complaints of physical fatigue between all groups. Mental fatigue and fatigability was equally common in CFS and affective patients, but only occurred in those neuromuscular patients who were also cases of psychiatric disorder. Overall, the CFS patients more closely resembled the affective than the neuromuscular patients. Attribution of symptoms to physical rather than psychological causes was the principal difference between matched CFS and psychiatric controls. The symptoms of "postviral" fatigue had little ability to discriminate between CFS and affective disorder. The fatigue in CFS appeared central in origin, suggesting it is not primarily a neuromuscular illness. The implications for research and treatment of chronic fatigue are discussed.

The clinical problem of patients with severe fatigue without obvious cause has received renewed attention in the professional literature, accompanied by intense media interest. Many of these patients are being diagnosed as "postviral" fatigue (or "chronic mononucleosis" in the USA[1]), whilst a patients' organisation, the *Myalgic Encephalomyelitis ("ME") Association,* has become Britain's fastest growing charity.

Nevertheless, there remains a lack of data on aetiology, nosology, characteristics, prognosis and treatment.[2] There is also no consensus about nomenclature. The term "chronic fatigue syndrome" (CFS)[3 4] has been proposed, as it is an accurate clinical description but has no aetiological implications. It will be used in this paper.

Most of the information on the aetiology of chronic fatigue states derives from case-control studies. Evidence of an increased rate of exposure to viral agents in cases, but not controls, has been found in some,[5 6] but not all, studies.[7] However, in these papers the diagnosis of a case ("postviral fatigue") has usually been made by knowledge of exposure (viral infection), thus violating the axiom that cases be selected independently of exposure, the central condition for conducting valid case-control studies.[8] Other studies have now begun to question the link between infection and chronic fatigue.[1 9 10]

The current study was concerned with the disease syndrome (chronic fatigue) irrespective of possible aetiology. It is therefore necessary to consider the key symptom, fatigue, since lack of information concerning the nature of fatigue[2 11] is an important reason for current confusion in case definition.

Fatigue as a symptom is both vague and subjective, even in the normal population.[12] As long ago as 1921 a Board of Inquiry concluded that an objective test for all forms of fatigue was an impossibility.[13] Fatigue is an accompaniment of a wide variety of diseases. In a UK community survey[14] 20% of men and 25% of women felt they "always feel tired". Community[15] and primary care studies in the USA[16 17] have similar findings. Patients with fatigue that cannot be explained on simple grounds are a major health problem.[18]

The pathophysiological mechanisms responsible for fatigue may be divided into central and peripheral

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Received 13 December 1988.
Accepted 6 February 1989

causes.[19 20] The peripheral causes are clearer, including such illnesses as myasthenia gravis, metabolic myopathies etc. The pathogenesis of fatigue in central disorders is less understood, and are assumed to include deficits of organisation, integration and motivation.

The origin of the fatigue in the postviral syndrome remains to be established. If the pathological process underlying CFS is muscular in origin, then by definition the fatigue will be of the peripheral type. There is evidence for a muscle disorder in CFS.[21 22] However, neither the MRI,[23 24] nor the muscle studies[25 26] have been replicated, especially when the effects of inactivity are taken into account. A report of an electromyographic abnormality[27] is also controversial, since the finding of increased jitter without impulse blocking cannot account for muscle fatigability. Others have demonstrated normal muscle function,[20 28] implying a central origin. However, the case for a central origin currently rests on the exclusion of peripheral causes rather than on positive evidence. No one has used the symptoms of fatigue (rather than neurophysiology) for this purpose.

The role of psychiatric disorder is obscure. Although most agree that symptoms of emotional disorder are the rule rather than the exception[29 30] little objective work has been undertaken. The only study using standardised interviews[31] found that 16 of 24 patients were current cases of major depression, whilst 12 of 24 had a history of affective disorder prior to the "fatiguing" illness. However, the diagnostic criteria employed included fatigue as a symptom of psychiatric disorder, thus introducing an unwanted circularity into the results.

The current study starts from the premise that although risk factors may exist, the aetiology of CFS remains unknown. All cases of fatigue seen in a non-psychiatric hospital without an acceptable diagnosis were therefore included. The aims of the study were to establish:

(1) The similarities and differences between fatigue of known central or peripheral origin.
(2) The nature of fatigue in patients with "postviral" fatigue.
(3) The role of psychiatric disorders in "postviral" fatigue.
(4) The role of symptom attribution.

Sample

The study was of three groups. The first included the cases of unexplained fatigue (CFS). Controls were chosen to represent "clean" examples of peripheral and central fatigue, and were therefore cases of peripheral neuromuscular and affective disorder respectively.

Group 1: All the neurological staff of the National Hospital for Nervous Diseases were asked to refer all new patients who satisfied the following criteria: (1) A primary complaint of fatigue, (2) An illness lasting six or more months, (3) No diagnosis reached after investigation ("Postviral" syndrome was not included as a diagnosis). (4) An absence of abnormalities on conventional neurological testing (muscle enzymes, nerve conduction studies, EMG, and muscle biopsy when performed), (5) Minimum age 18 years.

Fifty-one patients were referred during the 7 months of the study period. Three were subsequently excluded, as they were later diagnosed as multiple sclerosis, thyrotoxicosis and a familial myopathy respectively. (All the excluded patients felt they had "ME"). One patient refused to be interviewed, leaving a study group of 47.

Group 2 Patients with peripheral neuromuscular fatiguing (n = 33) illnesses seen at the National Hospital for Nervous Diseases. Seventeen had myasthenia gravis, eight myopathies, three Guillan-Barré syndrome and five a variety of rare genetic or metabolic muscle disorders. Neurological disorders with central involvement, such as multiple sclerosis, were excluded.

Group 3 Consecutive inpatients (n = 26) at a psychiatric hospital with major depression diagnosed by Research Diagnostic Criteria (RDC).[32]

Methods

All patients were given a standardised assessment. Eligible patients were contacted either at home by letter, or on the ward, and completed the following self-assessments before being seen by the researchers:

(1) General Health Questionnaire (GHQ-12).[33]
(2) Hospital Anxiety and Depression Scale (HAD).[34]
(3) Shortened (32 item) Somatic Discomfort Questionnaire.[35]
(4) A questionnaire recording subjective aspects of fatigue states constructed for this study (available from the principal author). It included 13 items recording potentially different aspects of fatigue, arbitarily divided into eight "physical" and five "mental" complaints (table 1). Replies were scored 0 to 2 for each symptom, representing same as usual, worse and much worse than usual. The results were listed under "physical" or "mental" symptoms, giving a maximum score of 16 (physical) and 10 (mental). Additional items covered included precipitating and alleviating factors, diurnal variability, pain, and functional impairment.
(5) Attribution of symptoms, previous medical experiences and satisfaction with treatment were measured by six questions using a 5 point scale. For example, patients were asked to tick one of the following statements:

Table 1 *Fatigue symptoms assessed*

A.	PHYSICAL FATIGUE
1.	I get tired easily.
2.	I need to rest more.
3.	I feel sleepy or drowsy.
4.	I can no longer start anything.
5.	I am always lacking in energy.
6.	I have less strength in my muscles.
7.	I feel weak.
8.	I can start things without difficulty, but get weak as I go on.
B.	MENTAL FATIGUE.
1.	I have problems concentrating.
2.	I have problems thinking clearly.
3.	I make more slips of the tongue, or have problems finding the correct word.
4.	I have problems with eyestrain.
5.	I have problems with memory.

(1) My illness is a physical one.
(2) My illness is mainly physical.
(3) Both physical and psychological factors are involved with my illness.
(4) My illness is mainly psychological.
(5) My illness is psychological in nature.

Finally, self-diagnosis was recorded.

All patients were later interviewed (CFS & neuromuscular controls by SW; affective by RP) using the Schedule for Affective Disorder and Schizophrenia (SADS),[36] a standardised psychiatric interview developed to provide current and lifetime RDC diagnoses.

Results

1. Demographic Date (table 2)

The CFS patients were younger than both control groups. There was no difference in self-reported length of illness in CFS and neuromuscular controls, but both had been ill for a shorter time than the depressed group. Case-notes indicated that both the CFS and neuromuscular patients dated their illness from the onset of fatigue, whilst the depressed group tended to date it from the start of the current episode only, suggesting information bias.

Table 2 *Demographic details*

	CFS	*Neuromuscular*	*Affective*
Number	47	33	26
Age	37 (35·4–40·3)	47 (42·6–52·6)	45·04 (39·89–50·19)
Female (%)	63 (48–78)	57 (40–74)	56 (37–75)
Length of illness (in months)	67·24 (37·6–96·5)	75·47 (48·5–102·5)	36·67 (10·5–51·4)

95% C.I. in parentheses.
ANOVA (DF = 2) unless stated.

2. Patterns of fatigue

All patients were severely physically fatigued. There was no difference in total fatigue scores between CFS and affective groups, but both were significantly more fatigued than the neuromuscular cases (table 3, fig 1). However, the differences were not substantial. In contrast mental fatigue was equally prominent in the CFS and affective group, but markedly less in the neuromuscular controls (fig 3, table 3).

A proportion of the CFS and neuromuscular patients fulfilled criteria for psychiatric disorder (see later). Dividing the groups according to the presence of psychiatric disorder had little effect on the rates of physical fatigue (fig 2), with only CFS:RDC case being significantly different from all other groups (ANOVA:F = 3·587; p = 0·01; multiple range test, least significance difference procedure with level of significant set at 0·01). However, the pattern of mental fatigue altered substantially (fig 4). The rate of mental fatigue in neuromuscular patients who were also cases of psychiatric disorder was not similar to other groups, whilst those with neuromuscular disease showed virtually no mental fatigue (F = 16·55; p < 0·00001; multiple range test, LSD procedure, 0·01 level of significance).

There were no interactions between duration of fatigue and measures of either mental or physical fatigue.

3. Precipitation of fatigue

A similar pattern emerged in the responses to questions asking "what brings on your fatigue?" (table 4). Precipitation by physical exercise occurred in the majority of CFS and neuromuscular cases, and in 56% of the affective controls. No change occurred when divided by the presence of psychiatric disorder. In contrast, fatigue precipitated by mental effort is ubiquitous in CFS and affective disorder, but only

Table 3 *Results of self administered questionnaires*

	CFS	*Neuromuscular*	*Affective*	*f value*	*signif.*
Physical fatigue	11·82(10·8–13·03)	8·28 (6·66–9·9)	10·35 (9·14–11·56)	6·215	0·003
Mental fatigue	5·84 (4·96–6·72)	2·42 (1·46–3·38)	5·5 (4·4–6·6)	15·669	<0·0001
GHQ	6·98 (5·82–8·14)	2·48 (1·3–3·66)	10·53 (9·47–11·53)	32·442	<0·0001
HAD	16·08 (12·9–19·25)	11·04 (8·47–13·61)	26·89 (22·91–30·87)	22·205	<0·0001
Somatic symptoms	14·8 (12·5–17·8)	7·81 (5·69–9·9)	11·71 (9·17–14·25)	9·455	0·0002

95% C.I. in parentheses.
ANOVA (DF = 2) unless stated.

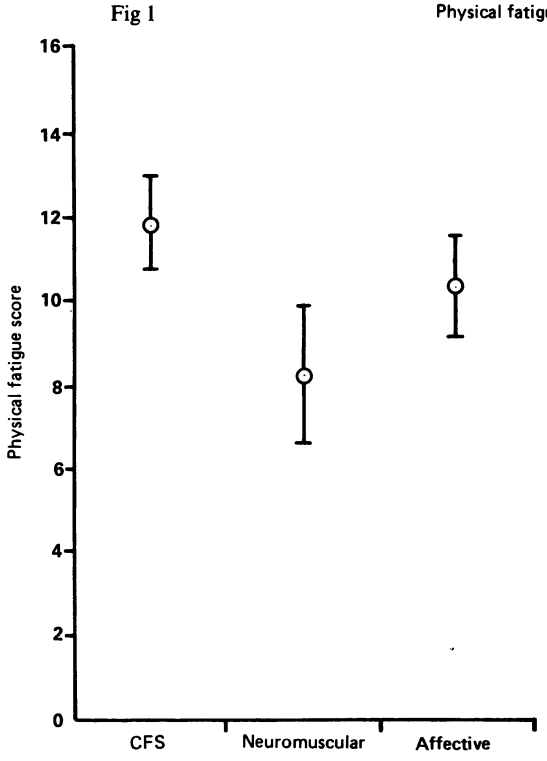

Fig 1 *Physical fatigue scores.*

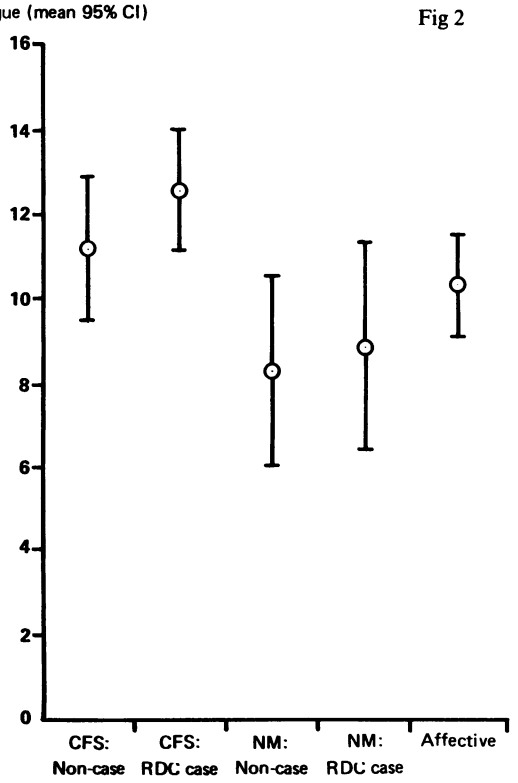

Fig 2 *The influence of psychiatric illness on physical fatigue scores.*

occurs in neuromuscular diseases in the presence of psychiatric disorder. There is an interaction between psychiatric caseness and mental fatigability in the neuromuscular but not in the CFS group (table 5).

4. Individual symptoms of fatigue

The next aim was to determine the differences, if any, between the many symptoms of fatigue (table 1). Principal components analysis of eight potential symptoms of physical fatigue across all groups gave a single factor solution, with the first factor accounting for 52% of variance. The rest descended in linear order from 11·5 to 3·1. The lowest factor loading for any symptom was 0·527 (feeling sleepy), and 0·585 (less strength), the others being over 0·79. Cronbach's alpha,[37] a measure of internal reliability, was 0·7484 (w = 0·0433). If each symptom was removed in turn, no significant change occurred in alpha (range 0·823–0·862). The same analysis of the five symptoms of mental fatigue gave a one factor solution, accounting for 68·7% of the variance. Cronbach's alpha was 0·871 (w = 0·028). Both physical and mental fatigue scores easily fulfilled the requirements for suggesting that a single construct underlies the response to the various questions.[38]

Table 4 *Precipitation of fatigue*

	% (95% CI) with fatigue precipitated by effort (number)		
	Fatigue after physical effort	*Fatigue after mental effort*	*At rest*
CFS	96 (90–101) 45	89 (77–92) 41	46 (30–59) 21
Neuromuscular	91 (81–101) 30	45 (29–61) 15	27 (12–43) 9
Affective	56 (46–66) 14	80 (12–28) 20	48 (38–58) 12
chi squared	25·33	19·15	3·24
p value (2 tailed)	0·0001	0·0001	NS

Table 5 *Effect of psychiatric illness on mental fatigue*

Psychiatric status (RDC)	*Chronic fatigue syndrome*		*Neuromuscular disorders*	
	Case	*Non-case*	*Case*	*Non-case*
Fatigue on mental effort	31 (94%)	11 (85%)	11 (92%)	4 (19%)
No fatigue on mental effort	2 (6%)	2 (15%)	1 (8%)	17 (81%)
	Odds ratio = 2·81		Odds ratio = 46·75	

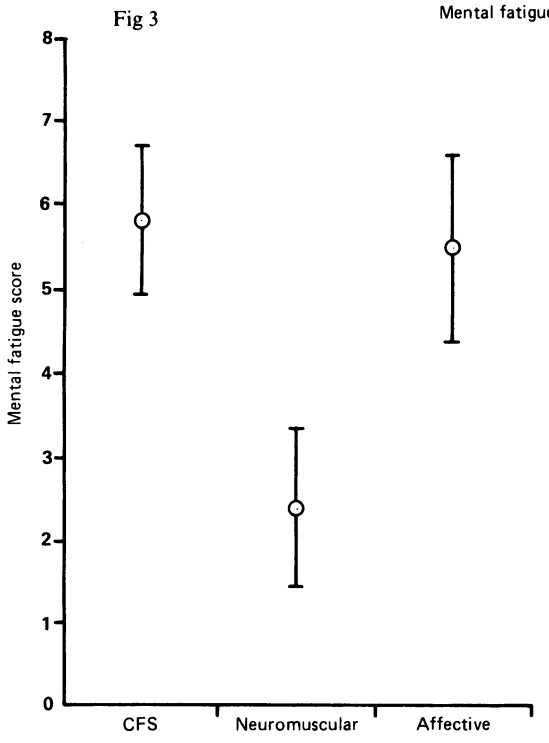

Fig 3 *Mental fatigue scores.*

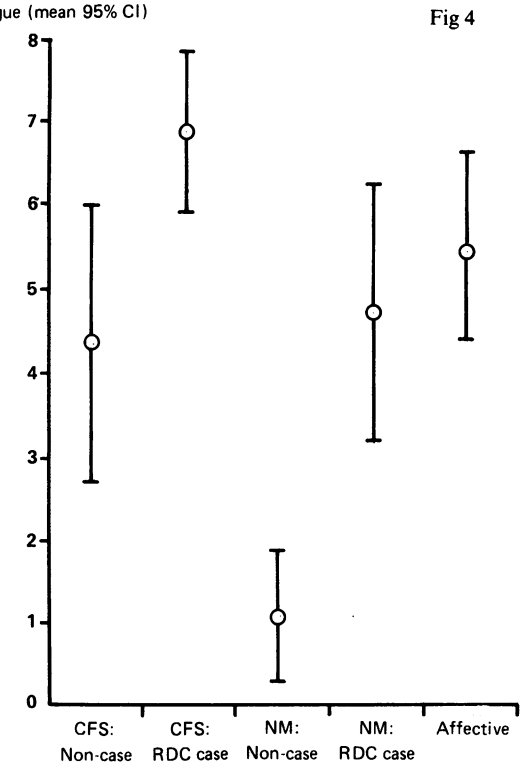

Fig 4 *The influence of psychiatric illness on mental fatigue scores.*

Principal components analysis of the physical and mental fatigue scores together gave a three factor solution after varimax rotation. Factor one (43% of variance) loaded strongly on physical fatigue (all above 0·61), factor 2 (17% of variance) on mental fatigue (all above 0·87), whilst the third factor loaded on eyestrain (0·78) and less strength (0·71), but only accounted for 8% of variance. This suggests that at least part of the constructs underlying physical and mental fatigue are different.

5. Psychiatric diagnoses in CFS (table 6)

RDC pychiatric diagnoses were applied to all patients. These criteria normally include fatigue as a symptom of several psychiatric illnesses, but for reasons explained above fatigue was not included as a symptom for this study. Despite this, 34 (72%: 95% CI 60–85%) of the CFS group were cases of psychiatric disorder, compared to 12 (36%: 95% CI = 20–53%) of the neuromuscular controls (chi squared = 10·8, p < 0·001 after Yates correction).

Table 6 *Psychiatric diagnoses (CFS)*

Psychiatric diagnosis (modified RDC)	
Major depression (definite or probable)	22 (47%)
Somatisation disorder	7 (15%))
Minor depression	1
Phobic disorder	2
Generalised anxiety disorder	1
Conversion disorder	1
All psychiatric diagnoses	34 (72%)
No psychiatric diagnosis	13 (28%)

Past psychiatric history was also rated by RDC criteria excluding fatigue. It was significantly more common in the affective controls (64%) than in the CFS (43%) or the neuromuscular patients (30%) (chi squared = 9·724; p = 0·0077). There was a possible ascertainment bias, as psychiatric history was more accurately detailed in the casenotes of the affective than the CFS or neuromuscular patients. Prior to the development of fatigue unexplained medical illness had occurred in 17 (36%) of the CFS group, rated by casenotes and history. Similar data were not obtained for the control groups.

6. Other symptoms (table 3)

GHQ scores were calculated traditionally (0011).[33] The CFS group were intermediate between the neuromuscular and depressed groups. The high absolute scores in CFS reflects the severity of illness in the depressed controls.

Anhedonia, the loss of pleasure, is the symptom whose presence is held to be the most effective way of separating mood disorder from the overlapping symptoms and consequences of physical illness.[39] Both self-report and observer ratings of anhedonia (SADS) showed significant differences between all three groups, the CFS patients lying midway between the affective and neuromuscular controls (Kruskal-Wallis oneway ANOVA; chi-squared = 13·13; p = 0·0008).

The number of somatic symptoms were significantly different between all three groups (table 3). These were most frequent in the CFS patients (LSD procedure, significance level = 0·05). Comparing CFS and depressed groups, only headache, eyestrain, tremor and muscle pain at rest were significantly more common at the 5% level in CFS, and given the number of comparisons this may be random sampling error. There were no differences in many of the symptoms held to be specific for "postviral" fatigue, such as hypersomnia, sensitivity to noise, gastrointestinal disturbance, and particularly muscle pain after exercise. The latter occurred in 83% (95% CI = 69–97%) of CFS patients and 67% (95% CI 49–85%) of the depressed patients.

7. Classification of CFS

The control groups were chosen to provide two different types of fatigue against which CFS patients could be compared. For this purpose three group discriminant function analysis of symptoms was performed. Using only control cases (and not CFS) all current symptoms (physical fatigue score, mental fatigue score, GHQ, HAD, somatic score, anhedonia and mental and physical precipitation) were entered simultaneously. Agreement with predicted group membership was as follows: neuromuscular only, 90%; neuromuscular cases with concurrent psychiatric (RDC) disorder, 91%; affective controls 100%. When these results were applied to the CFS cases four (9%) were classified with neuromuscular non-RDC cases, 20 (44%) with neuromuscular cases who were also psychiatrically ill, and 21 (47%) of the CFS cases with the affective group.

8. Attribution of symptoms

On symptoms alone 47% of the CFS sample are thus indistinguishable from the affective controls.

Table 7 *Attribution of illness (Matched cases)*

	CFS	*Affective*
Physical causes	18	3
Psychological causes	1	19

Fisher's exact = 0·0002.

However, the two groups are not identical, since one was assessed in a major neurological centre, the other in a psychiatric hospital. The major difference between the two groups was the pattern of symptom attribution. There was an almost complete separation (table 7), with 18/21 of those CFS cases classified with affective disorder believing their illness had a physical cause (in the entire CFS group the figure was 39/47). The opposite occurred in the affective controls. Three CFS and four controls felt their illness to have both physical and psychological causes. The results were identical if the comparison was between those cases (22) of CFS clinically diagnosed as major depression and depressive controls.

9. Exposure to viruses

Seventy-two percent of the CFS group reported that their illness had been associated with a viral illness, compared with 42% of the neuromuscular and 21% of the depressed controls (chi squired = 19·47; p = 0·0001). Using more rigorous criteria (serological proof of a past viral illness), this figure fell to 33%. However, there was no difference in any symptoms if the sample was divided according to a history of viral exposure, whether by self-report or serological criteria. No single organism was implicated, those involved included enterovirus, EBV, influenza, hepatitis A and toxoplasmosis.

10. Missing data

Checks were made on all requests for muscle biopsies and myometry. During the study period seven patients were seen at the hospital who appeared to fulfil the criteria but were not referred. Case-note review showed that three would have satisfied RDC criteria for major psychiatric illness, one would not, whilst there was insufficient information in three to decide. The sample thus consisted of 88% of those eligible, but it appears that missing cases resembled those assessed.

Discussion

1. The chronic fatigue syndrome

Physical fatigue and fatigability are prominent in CFS, but also in depressive and neuromuscular disorder, implying that subjective complaints of physical fatigue have little use diagnostically. This is not true of mental fatigue. It is equally common in both depression and CFS, but only occurs in peripheral neuromuscular disorders if there is coexisting psychiatric illness. Mental fatigue is found in CFS irrespective of psychiatric disorder, suggesting it is not simply due to lack of diagnostic precision. The detailed analysis of symptoms indicates there may be some distinction between mental and physical fatigue in general, but not between individual symptoms. In this type of sample the

distinction between weakness and fatigue may be of more importance to clinicians than patients.

These results support the existence of a chronic fatigue syndrome, if it is defined by mental and physical fatigue associated with mental and physical effort. Only four out of 47 (8%) patients described a physical fatigue that was not associated with mental fatigue. These features did not occur in peripheral neuromuscular disorders unless central disorder, indicated by psychiatric illness, was also present, suggesting that the fatigue in CFS results from a central mechanism. The central origin can be inferred from the symptoms alone. In most patients any abnormalities in muscle structure or function may therefore be either epiphemonena of the disease process, and not directly linked to symptoms, or result from physical inactivity.

However, a chronic fatigue syndrome is not exclusive to chronic "postviral" fatigue. The same pattern of central fatigue was found in the depressed controls. Unlike the fatigue group, these were not selected by a complaint of fatigue, but were consecutive admissions to a psychiatric hospital. The results confirm that fatigue is a frequent accompaniment of major depression, but also suggest a considerable overlap between CFS and affective disorder.

The first possibility is that the affective changes are "simply a reaction to a chronic state of ill health".[40] However, the comparison between the rate of psychiatric disorder in the neurological controls, which was in keeping with previous studies,[41] and the CFS patients, shows that disability alone cannot account for the significantly higher rate of psychiatric disorder in the latter, who had been ill for an equivalent length of time. Furthermore, increased length of illness was not associated with increased physical fatigue or mental illness.

An alternative hypothesis is that all cases of CFS can be explained by disorder of mood. Forty-seven percent were indeed cases of affective disorder using internationally accepted diagnostic criteria, modified to exclude fatigue (conventional methods would give a higher figure), but 25% had other psychiatric diagnoses, and 28% had no psychiatric disorder. Depression is thus not the sole explanation for these findings. However, 10 out of 13 without formal psychiatric disorder had disturbances of sleep and/or appetite. Hypothalamic dysfunction is important in disorder of mood[42] and a similar "final common pathway" may exist in CFS. CFS is a heterogenous condition: depressive illness is a sufficient, but not necessary, explanation.

This study supports the finding in two American studies of a close association between unexplained fatigue and emotional disorder. In primary care[16] symptoms of depression were found in 56% of the fatigued sample, but no diagnoses were made. Conventional measures of psychopathology accurately discriminated between fatigued patients and controls in 92% of cases. Of 135 self-referrals to a special fatigue clinic in a university hospital[43] 67% had psychiatric diagnoses (of which the majority had affective disorder), 3% had medical diagnoses, leaving 25% unexplained. Despite differences in population and design, these figures are close to our own.

We have also shown that attribution of symptoms is a major confounding factor. In those cases of CFS who could not be distinguished from depressed controls by any measure, the patient's view of the origin of their symptoms was the major factor determining whether they were seen in a general or psychiatric setting. The self-diagnosis (and perhaps medical diagnosis) of "ME" or "postviral fatigue" appears more influenced by views on physical or psychological causation than any particular symptom.

It is not our intention to adjudicate between the opposing views of physical or psychological aetiology. With the expanding knowledge concerning the biological basis of many psychiatric illnesses such a division becomes increasingly meaningless. However, both patients, and some doctors, continue to insist on such distinctions. It is instead our purpose to point out the serious consequences that result from this division. Not only will this lead to bias in research based on general hospital samples (as most has been), but it also suggests that many patients are being deprived of effective treatment.

The role of infection in the pathogenesis of chronic fatigue remains obscure. Certainly the majority of "CFS" patients felt their illness had commenced with a "virus" (54% were members of the "ME" Association). However, no symptomatic differences emerged between those with or without history or evidence of a precipitating viral illness. Furthermore, no specific agent was identified, as has been reported elsewhere.[21 44] These results do not exclude an aetiological role for infectious agents, but are not compatible with a specific postviral fatigue. Viruses may not be either necessary nor sufficient for the development of CFS. Instead, it suggests that the link, if any, between virus and fatigue operates via recognised psychiatric disorder in the majority of cases, and by a still unknown central mechanism in even more cases. These findings should help focus future research (and treatment) on more profitable lines of inquiry.

The symptoms of "postviral" fatigue

Overall, the symptoms held to be characteristic of CFS[5 21 30 45 46] lacked specificity. Fatigue after exercise occurred in nearly all the CFS patients, but was also present in over half the depressed controls, as was myalgia. The symptoms of physical fatigue had no

discriminating value between any of the groups. Although mental fatigue and fatigability did discriminate between CFS and neurological patients, it was as common in the depressed group. The poor specificity of the symptoms of CFS emphasises the limitations of much of the published research, since symptoms alone are not sufficiently reliable to permit the accurate case definitions required for sophisticated research. Our results show the substantial variation in the definitions of both exposure (that is, viruses) and disease (CFS). The study confirms serious doubts about the usefulness of "normal" controls in investigations into CFS.[1]

The study is limited by the sample chosen. It was restricted to specialist hospital practice, as such patients have formed the basis of most of the published work in CFS. It cannot be applied to primary care. However, this meant that patients had been ill for several years. It has been argued that different aetiological factors operate at different stages of chronic fatigue,[47] and that factors which are relevant at the commencement of illness are not the same as those responsible for chronicity. Short-term prospective studies have elegantly demonstrated that psychological disorder is a predictor of length of illness following influenza,[48] and EBV.[49] The current study demonstrates the importance of psychiatric illness in fatigue states of longer duration.

We thank all the medical staff at the National Hospital for their unstinting cooperation. We also thank J Morris (Institute of Neurology), M Ron, M Wiles & R Dolan (National Hospital), A David, G Lewis & A Pelosi (Institute of Psychiatry) and P White (St Bartholomew's Hospital).

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