GENERAL PRACTICE

Population based study of fatigue and psychological distress

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Abstract

Objectives-To determine the prevalence of fatigue in the general population and the factors associated with fatigue.

Design—Postal survey. Setting—Six general practices in southern England. Subjects-31651 men and women aged 18-45 years registered with the practices.

Main outcome measures-Responses to the 12 item general health questionnaire and a fatigue questionnaire which included self reported measures of duration, severity, and causes of fatigue.

Results-15283 valid questionnaires were returned, giving a response rate of 48.3%, (64% after adjustment for inaccuracies in the practice registers). 2798 (18.3%) of respondents reported substantial fatigue lasting six months or longer. Fatigue and psychological morbidity were moderately correlated (r=0.62). Women were more likely to complain of fatigue than men, even after adjustment for psychological distress. The commonest cited reasons for fatigue were psychosocial (40% of patients). Of 2798 patients with excessive tiredness, only 38 (1.4%) attributed this to the chronic fatigue syndrome.

Conclusion—Fatigue is distributed as a continuous variable in the community and is closely associated with psychological morbidity.

Introduction

Community surveys have shown that fatigue is common in developed countries. A British survey of those attending general practice found that 10.2% of men and 10.6% of women had had substantial fatigue for over a month.1 Despite its prevalence, however, surprisingly few data exist on the demographic and social associations of fatigue.²

In recent years fatigue has attracted renewed attention, largely because of the prominence given to the chronic fatigue syndrome, also known as postviral fatigue or myalgic encephalomyelitis. However, controversy exists concerning not only the relative contributions of infective and psychological risk factors but the classification of the syndrome itself. These disputes cannot be resolved without sound community studies.3

Nearly all studies of chronic fatigue syndrome have been conducted in tertiary referral settings, where the typical patient is a young adult, usually a woman, with a professional job. Most patients trace their illness to an infective trigger but also fulfil criteria for a psychiatric disorder.⁴⁷ The infective and psychiatric characteristics may, however, be the result of referral patterns and illness behaviour and not intrinsically related to the chronic fatigue syndrome.

We conducted a large community survey to determine the level of fatigue and psychiatric morbidity in a population, to explore the association between fatigue and psychological distress, and to identify what fatigue is commonly attributed to.

Subjects and methods

We sent questionnaires to all patients aged 18 to 45 years registered with selected practices. We recruited six practices to the study, three from London and three from rural or semirural settings, two of which belonged to the Medical Research Council general practice research framework.

Two practices (subsequently referred to as practice 1) were working from the same health centre in south London in a mixed urban community with a large amount of temporary accommodation. Practice 2 was an inner city London practice where most patients were socially deprived. The third practice was located on the Surrey-Hampshire border with patients predominantly in socioeconomic classes II and III. Practice 4 was in an urban area of a south coast port, and the last practice was in a Somerset village, with a static close knit community and many stable families. The total number of patients aged 18-45 registered with the practices was 31651 (15222 men, 16429 women).

Fatigue was assessed with a self reported questionnaire (the fatigue questionnaire), which was developed for a hospital study of the chronic fatigue syndrome⁷⁸ and was refined during a validation study conducted in primary care.⁹ It consists of 11 items covering the physical and mental aspects of fatigue. Additional questions concern the duration of fatigue, the percentage of time during the day the respondent felt tired, and two questions on muscle pain at rest and after exercise. The response to the questions on muscle pain were summed to give a total score. Respondents were also asked "why do you think you are feeling tired?" We also included the 12 item general health questionnaire.10 The general health questionnaire is a well validated measure of psychological morbidity; those scoring above the predefined cut off have an increased chance of suffering from a psychiatric disorder. Both questionnaires use similar responses, usually of the form not at all, same as usual, more than usual, and much more than usual.

Two systems of scoring were used for both questionnaires, traditional (0,0,1,1) and Likert (0,1,2,3). Responses to the presence or absence of muscle pain at rest and on exercise were scored 0 or 1.

We posted the questionnaires in November 1991. Non-responders were sent a second questionnaire four weeks later. In four practices a random sample of 100 persistent non-responders was followed up by telephone or personal visits and the reasons for nonresponse determined. Addresses were checked with the electoral register, and telephone numbers were taken from notes within the practice or telephone directories. In one of the four practices it was considered inadvisable for the research nurse to make home visits. The last practice did not allow any follow

STATISTICAL ANALYSIS

Statistical analysis was performed with the spss

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BMJ 1994;308:763-6

program. We applied parametric statistics since with large numbers the distribution of responses to both questionnaires follows a normal distribution if Likert scoring is used.

Results

We received 15 283 completed replies, 6532 from men and 8757 from women. This was a response rate of 48.3%. Table I shows the response rate for each practice. The lowest rates were obtained in the two inner London practices (43% and 37.5% respectively). A total of 387 incomplete questionnaires were returned and were discarded from the analysis. As others have found in similar surveys,¹¹ non-responders were more likely to be men (53%) and were slightly younger than responders (mean age 30.8 (95% confidence interval 30.7 to 30.9) years for non-responders, 32.4 (32.3 to 32.5) years for responders; F=436.66, df=1, P<0.001).

The main reason for non-response was change of address. In the four practices surveyed 19%, 39%, 46%, and 69% of non-responders did not receive the questionnaire because they have moved house. The differences between the practices reflect the greater social mobility in the inner city practices. Adjustment for those with wrong addresses or who had moved and extrapolation of this data to the entire sample (arbitrarily assuming an error rate of 19% for the fifth practice in which no data could be obtained) gave an adjusted response rate of 64%.

FINDINGS OF QUESTIONNAIRES

Figures 1 and 2 show the frequency distribution of fatigue questionnaire and general health questionnaire scores. In all, 5799 (38%) patients had a score above the cut off established in a primary care validation study for substantial fatigue,9 and 5621 (36.7%) scored above 3/4 (traditional scoring system) in the general health questionnaire, which is the cut off for psychological disorder. A total of 2798 (18.3%) were substantially fatigued for six months or longer. Scores in the fatigue and general health questionnaires were moderately correlated (r=0.62, 95% confidence interval 0.61 to 0.63) with a linear trend between fatigue score and mean general health questionnaire score (fig 3). Mental and physical fatigue scores were also significantly correlated: (men r=0.54, 0.52 to 0.56; women r = 0.54, 0.53 to 0.55).

Age was very weakly correlated with scores on both the fatigue (r=0.08, P<0.01) and the general health questionnaires (r=0.03; P<0.01). Fatigue scores in women increased with age but only slightly. The mean fatigue score was 24.1 (95% confidence interval 24.0 to 24.2) for men and 25.2 (95% 25.1 to 25.3) for women the difference in means being 1.1 (0.96 to 1.24). The





FIG 3—Mean and 95% confidence interval score for general health questionnaire according to fatigue score

mean general health questionnaire score was 24.7 (24.6 to 24.9) for men and 26.2 (26.1 to 26.4) for women, the difference in means being 1.5 (1.3 to 1.7). Because of sample size these sex differences were highly significant (independent t test P<0.0001) but are probably not clinically important.

We explored the relation between sex, fatigue, and general health questionnaire score with analysis of variance. Women had significantly more fatigue than men (F=45.41, df=1, P<0.001). Psychiatric morbidity was a confounding variable since community surveys usually report that women have higher psychological morbidity than men, as confirmed in this study. Stratifying by psychological morbidity on the basis of general health questionnaire caseness did not remove the excess of fatigue in women. This was confirmed by an analysis of variance using the general health questionnaire score as a covariable. The effect of sex remained significant (F=45.51 P=0.001).

We asked all patients the reasons why they were tired (table II). Most patients gave one reason but where there were two or more the first was taken to be the most important. The commonest attribution was psychosocial, such as work, family, and lifestyle. The next most popular category was psychological distress (usually anxiety or depression), followed by physical causes (for example, surgery, anaemia). The last major category consisted of "other" causes, which were mainly environmental (including the weather and pollution). Thirty eight people described themselves as having the chronic fatigue syndrome. More detailed follow up of these patients will be reported elsewhere. All belonged to social classes I, II or IIIa and 30 were women. Patients with a self diagnosis of the chronic fatigue syndrome had the highest mean fatigue scores, followed by those who attributed their fatigue to pregnancy, physical, and psychological causes respectively. Psychosocial attributions were associated with the lowest mean fatigue scores.

A total of 2107 (13.8%) subjects complained of

Practice

1

234

5

TABLE I-Response rates in

No of

eligible

patients

11270

7999

6152

4932

1838

No of

respondents

(%)

4846 (43) 3000 (37·5)

3888 (63.2)

2732 (55.4)

1108 (60.3)

participating practices

	No (%) of patients			
No reply	3042 (19·9)			
Pregnancy	289 (1.9)			
Psychological	2552 (16.7)			
Psychosocial	6123 (40-1)			
Physical	2247 (14.7)			
Other	992 (6.5)			
Chronic fatigue syndrome	38 (0·2)			
Total	15283 (100.0)			

muscle pain at rest, and 3286 (21.5%) complained of muscle pain after exercise. There was a linear relation between general health questionnaire score and proportion complaining of either muscle pain at rest or after exercise (χ^2 test for trend, P<0.001). With a cut off of 4 for the general health questionnaire 19% (2387) of non cases complained of muscle pain at rest or after exercise compared with 40% (1088) of cases (odds ratio=2.8; 95% confidence interval 2.7 to 2.9).

Table III shows the effect of using some of the current criteria for the chronic fatigue syndrome¹² on the prevalence of fatigue and its relation to psychological morbidity. The criteria include the effect of duration, proportion of time fatigued, and the presence of myalgia. Each restriction progressively decreased the prevalence of arbitrarily defined fatigue states but increased both the proportion of cases on the general health questionnaire and the female:male ratio.

Discussion

Studies of the chronic fatigue syndrome have been based in either general practice or tertiary referral centres. We conducted a large community survey of fatigue in which the participating practices were chosen to reflect a wide spectrum of social and geographical settings.

The overall response rate of 48.3% was disappointing, and was largely due to the low rates obtained in the inner London practices. However, others have shown, again in south London, that the family health services authority registers are only 75% accurate because of the young and relatively mobile population in the inner city.13 In our study 109 out of the 200 non-responders randomly followed up in the London practices had moved or had non-existent addresses. Hence only three quarters of the questionnaires for the London sample reached their destination, reducing the true sample size. Non-responders who received the questionnaire almost certainly differed in both fatigue and psychological distress, introducing a possible response bias, but a non-response bias due to change of address seems less likely. Overall the adjusted response rate, although far from ideal, is comparable with that in other community postal surveys.11 14

The results support the concept of a continuum of fatiguability, as already suggested by data from a primary care study in the United Kingdom and a community survey in the United States.¹² The chronic fatigue syndrome, defined only by symptoms, disability, and duration, may represent a morbid excess of fatigue rather than a discrete entity, just as high blood pressure and alcohol consumption are morbid ends of normal spectrums. Hence the definition may have arisen as a result of referral patterns to specialists.

In our survey 18% of respondents complained of excessive fatigue for six months or longer, confirming the importance of fatigue as a symptom in the community. The demographic associations found in this

TABLE III—Effect of different criteria for chronic fatigue syndrome on prevalence of fatigue syndrome and its relation to psychological morbidity

Criteria (fatigue score >4 and at least six months duration)		No of cases on general health questionnaire			
	No (%) of patients (n=15 283)	Total (%) (n=5621)	Women (n=3574)	Men (n=2047)	F:M Ratio
Fatigued 50% of time	722 (4.7)	442 (61·2)	270	172	1.6
Fatigued 75% of time	634 (4·1)	465 (73·3)	312	153	2.0
Fatigued 100% of time	262 (1.7)	215 (82·1)	150	65	2.3
Fatigued 50% of time plus muscle pain+	321 (2.1)	200 (62.3)	119	81	1.5
Fatigued 75% of time plus muscle pain† Fatigued 100% of time plus muscle	333 (2.2)	268 (80·5)́	182	86	2.1
pain†	147 (1.0)	133 (90·5)*	97	36	2.7

* χ^2 test for trend. P<0.01.

 $Muscle pain = total muscle score \ge 1.$

Practice implications

- Fatigue is a common symptom in the community
- In this community survey symptoms of fatigue fitted a normal distribution
- Most patients with excessive fatigue blamed psychosocial factors for their symptoms. The chronic fatigue syndrome was mentioned by only 1%

• Fatigue and psychological morbidity were related and the association increased in those with prolonged or severe fatigue or with other symptoms such as muscle pain

study agree with previous data.² Women were more fatigued than men. Women also had more psychological disorder than men, but this finding did not explain the excess of fatigue in women. The relative risk of fatigue in women compared with men in our study was 1.3, identical to the relative risk found in a single general practice in this country,¹ and in a single general practice in Canada.¹⁵ The failure of both groups to find significant sex differences may reflect lack of power.

ASSOCIATION WITH PSYCHOLOGICAL MORBIDITY

We found an association between the number and severity of fatigue symptoms and psychological morbidity (fig 3). Two primary care studies have reported a close association between the symptoms of fatigue and either psychological morbidity¹⁶ or psychiatric diagnoses.¹⁷ Numerous tertiary care studies have found associations between chronic fatigue syndrome and psychiatric diagnoses.18 Muscle pain was also related to psychological morbidity, confirming the associations noted in a recent general practice study from Lancashire." We conclude not that fatigue is caused by psychological morbidity, but that the two conditions overlap. The concordance between fatigue and psychological morbidity, and between the chronic fatigue syndrome and psychiatric disorder, is inevitable given the similarities of the criteria and measures used to define them.

Although this is not a study of the chronic fatigue syndrome, it does give some information about it. Firstly, self diagnosis of the chronic fatigue syndrome is extremely uncommon even among those with fatigue, accounting for only 1% of those with significant fatigue and 0.2% of the entire sample. Self diagnosis of the syndrome was associated with being female, high social class, and high levels of both fatigue and psychological morbidity.

Secondly, we measured two factors included in the current consensus criteria for chronic fatigue syndrome (duration of fatigue and percentage of time fatigued),¹¹ as well as the presence of myalgia, which is thought to be characteristic of the syndrome in Britain. Application of each of these criteria reduced the prevalence of a fatigue syndrome but increased the association with psychological morbidity. Thus 38% of the sample complained of excessive fatigue, but in only 1% had this lasted for more than six months, been experienced all the time, and been associated with myalgia. Among this group 90% were probable cases of psychiatric disorder, and women were over represented. This pattern confirms that increasing the number of restrictions in the definition of chronic fatigue syndrome does not reduce the association with psychological morbidity but has the opposite effect.¹⁹ Future studies will look at the development of post infectious fatigue in this cohort.

We thank the study nurses Melanie Brown, Julie Dennison, Sue Fox, Brenda Hinton, Vivien Hobos, Margerie Peers, and Dawn Baker and the general practitioners and staff of the participating health centres Jenner Health Centre, London SE23; Hurley Clinic, London SE5; Yateley Medical Centre, Yateley, Surrey: Rosemary Medical Centre, Poole, Dorset, and Mendip Country Practice, Somerset. The last two practices are members of the Medical Research Council general practice research framework. We are also grateful for the help of Peter Turk, Charing Cross Hospital Medical School, and David Blackett with computing. The study was supported by Linbury Trust, with additional support from Private Patients Plan and British United Provident Association.

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(Accepted 14 January 1994)

THE NOBEL PRIZES

Well done, the judges

While Ascot, Mothering Sunday, and the Eurovision Song Contest thrive as ever before, another great annual diversion is surely in terminal decline-the sport of berating the Nobel prize authorities for the choice of scientists to receive their unique, highly revered distinction. In just a few years the wisepersons of the Karolinska Institute (in the case of the physiology or medicine prize) and the Royal Swedish Academy of Sciences (the chemistry and physics awards) have largely swept off the stage a familiar trio of autumnal grumblers. They have seen off those who argued that an accolade had gone to scientist A when scientist B had made the more crucial advance, those who bewailed the aeons of time between discovery and reward, and those who used to point out that the work did not match Alfred Nobel's wishes anyway.

After 92 years, it seems, the Nobel authorities really are managing to meet all reasonable criteria for their benison. The result is a most agreeable balance between the recognition of fundamental and applied research, and between immediate plaudits where the merits are blatantly obvious and judicious judgments regarding work that is more distant in time and poses more serious difficulties of adjudication.

Consider some recent recipients. In 1989, when the chemistry prize went to Sidney Altman of Yale University and Thomas Cech of the University of Boulder, Colorado, for showing that RNA molecules can act as enzymes, the work was still brand new and there were no challenges regarding the choice of names. Science reported that molecular biologists and chemists alike hailed the award as "almost inevitable." The same could be said of the 1991 physiology or medicine prize, given to Erwin Neher of the Max Planck Institute for Biophysical Chemistry in Gottingen and Bert Sakmann of the Max Planck Institute for Medical Research in Heidelberg, who established that cell membranes have individual ion channels for the passage of tiny electric currents. Their work was still hot news at the time and has generated an enormous portfolio of further biological and medical studies.

Even sizeable intervals between a piece of research and the call to Stockholm are no longer so outrageous that they provoke criticism. For example, the decision to confer the 1990 prize for physiology or medicine on Joseph Murray of Harvard Medical School and Donnall Thomas of the Fred Hutchinson Cancer Research Center in Seattle was widely welcomed for two reasons. It reflected a canny judgment over who to spotlight as the crucial pioneers in the crowded and competitive field of organ transplantation. And, despite the 30 to 40 year delay in recognition, it reinstated clinical research, alongside more fundamental work, as worthy of science's greatest accolade. Likewise, when Edmund Fischer and Edwin Krebs, both of the University of Washington, became the laureates in 1992, the phenomenon for which they were honoured, reversible protein phosphorylation, was attracting renewed attention because abnormalities in the process are implicated in a wide range of diseases, from diabetes and asthma to cancer and myotonic muscular dystrophy.

And who could quibble, on grounds of immediacy, fundamental significance, and practical importance, with the 1993 names? The prize went to Richard Roberts and Philip Sharp, of New England Biolabs and the Massachusetts Institute of Technology respectively, for their demonstration that genes are not continuous stretches of DNA but are broken up by introns. "In terms of the molecular biology underlying disease, it has opened up a whole new area, not just in understanding the basic mechanism but also the variations of genetic disease," Sir David Weatherall commented in *Nature*.

The work of the chemistry prizewinners was similarly far reaching—the development of site directed mutation by Michael Smith of the University of British Columbia and of the DNA-amplifying polymerase chain reaction by Kary Mullis, now a freelance boffin. The former facilitates the rewriting of genetic programmes to create novel proteins—for example, new haemoglobins and more stable enzyme detergents. The latter is revolutionising medical diagnosis and forensic investigation, facilitating the retrieval of DNA fragments from insects embedded in 20 million year old amber, and spawning fantasies such as those of *Jurassic Park*.

There was insuperable difficulty in the dynamite inventor's instruction, published in his 1885 will, that Nobel prizes would be distributed to "those who, during the preceding year, shall have conferred the greatest benefit on humanity." Nevertheless, it's clear that the intellectual distinction of the science now being recognised is matched by its importance for humankind and indeed terrestrial wellbeing. This has by no means always been the case in the past.—BERNARD DIXON is a freelance science writer