Psychological Medicine, 1999, **29**, 863–868. Printed in the United Kingdom
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Fatigue and psychiatric disorder: different or the same?

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ABSTRACT

Background. Fatigue and psychiatric symptoms are common in the community, but their association and outcome are sparsely studied.

Method. A total of 1177 patients were recruited from UK primary care on attending their general practitioner. Fatigue and psychiatric disorder was measured at three time points with the 12-item General Health Questionnaire and the 11-item Fatigue Questionnaire.

Results. Total scores for fatigue and psychiatric disorder did not differ between the three time points and were closely correlated (r around 0·6). The association between non-co-morbid ('pure') fatigue and developing psychiatric disorder 6 months later was the same as that for being well and subsequent psychiatric disorder. Similarly, having non-co-morbid psychiatric disorder did not predict having fatigue any more than being well 6 months previously. Between 13 and 15% suffered from non-co-morbid fatigue at each time point and 2·5% suffered from fatigue at two time points 6 months apart. Less than 1% of patients suffered from non-co-morbid fatigue at all three time points.

Conclusions. The data are consistent with the existence of 'pure' independent fatigue state. However, this state is unstable and the majority (about three-quarters) of patients become well or a case of psychiatric disorder over 6 months. A persistent, independent fatigue state lasting for 6 months can be identified in the primary-care setting, but it is uncommon – of the order of 2·5%. Non-co-morbid (pure) fatigue did not predict subsequent psychiatric disorder.

INTRODUCTION

Fatigue is one of the commonest symptoms encountered in medical practice. Typically, a quarter of people in community and primary-care studies are currently fatigued (Lewis & Wessely, 1992). The prevalence of chronic fatigue, arbitrarily defined as fatigue enduring for longer than 6 months, is slightly less common with typical findings being about a fifth in the community or primary-care setting (Wessely, 1995).

Fatigue is frequently associated with psychiatric disorder in studies conducted in both primary and specialist care. Around three-quarters of primary-care attenders with chronic fatigue can be given a diagnosis of psychiatric disorder, while in specialist care approximately three-quarters of patients seen with a diagnosis of one of the variously defined chronic fatigue syndromes also meet criteria for a psychiatric disorder – chiefly depressive disorder in half and anxiety or somatization disorders in the remaining quarter (Wessely & Powell, 1989; Wessely, 1995). Uncertainty regarding the relationship between psychiatric disorder and fatigue persists partly due to a lack of longitudinal studies in the community.

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https://doi.org/10.1017/S0033291799008697 Published online by Cambridge University Press

The purpose of this paper is to examine the relationship between psychiatric disorder and fatigue and the outcome of non-co-morbid ('pure') fatigue in a primary-care setting. Two particular questions are addressed: first, does an independent fatigue state (e.g. such as neurasthenia) exist; and secondly, if such a fatigue state does exist independently, how stable is it over time?

METHOD

This work was done as part of a study into the prevalence of chronic fatigue syndrome in the community setting and its relationship to viral infection (Pawlikowska *et al.* 1994; Wessely *et al.* 1995, 1996).

Subjects and procedure

Questionnaires were posted to all patients aged 18 to 45 years registered with selected practices. Six practices were recruited to the study, three from London and three from rural or semi-rural settings. Two practices were in the same health centre in South London, an inner-city area with social deprivation. The third practice was located on the Surrey/Hampshire border with patients predominately in socio-economic classes II and III. The fourth was in an urban area of a south coast port, and the last was in a Somerset village with a stable population. The total number of patients aged 18 to 45 registered with the practices was 31651 (15222 men and 16429 women).

The sample used in this paper was the control group in the study of post-viral fatigue (Wessely *et al.* 1995). These subjects provide a sample of general practice attenders who have been measured on three occasions with regard to both psychological and fatigue symptoms. In that study, on attending his or her general practitioner (GP) with a viral infection (the exposed group) the next consecutive patient (the control group) was recruited, completed questionnaires and followed up 6 months later. In this study, for the control subjects only, the scores on the GHQ and the Fatigue Questionnaire (FQ) at three time points were analysed: stage 1 included the scores of the postal survey in the community sample, stage 2 the scores when the patient presented to his or her GP and stage 3 the scores at 6 months follow-up. The length of time between the first two stages varies between 1 to 12 months.

Fatigue was measured with a self-report questionnaire (Fatigue Questionnaire, Chalder *et al.* 1993), which was developed for a hospital study of chronic fatigue syndrome (Butler *et al.* 1991) and validated in primary care (Chalder *et al.* 1993). It consists of 11 items covering the physical and mental aspects of fatigue.

Psychological morbidity was assessed using the 12-item general health questionnaire (GHQ) (Goldberg & Williams, 1988). This questionnaire is well validated as a measure of psychological morbidity, those scoring above a predefined score have an increased chance of suffering from a psychiatric disorder.

Both questionnaires use similar responses: not at all; same as usual; more than usual; much more than usual. Traditional scoring (0,0,1,1), Likert scoring (0,1,2,3) and a 'caseness' threshold of 4 or higher on traditional scoring were used for both questionnaires. The caseness threshold used is high, and is likely to predict very symptomatic patients (Goldberg & Williams, 1988). Patients were allocated to four groups of caseness: (1) well (no caseness); (2) pure fatigue (FQ only case); (3) pure psychiatric disorder (GHQ only case); and (4) co-morbid (GHQ and FQ caseness).

Statistics

Statistical analysis was performed using the SPSS computer program. Likert scoring for GHQ and FQ produces approximately normal distributions in community samples allowing parametric statistics to be used. Differences in means and in proportions between time points were assessed by one-sample *t* test and matched-pair chi-squared test, respectively. Associations were assessed by Pearson's correlation coefficient for continuous variables.

The association between each of the three clinical case categories at stage 2 (i.e. fatigue only, GHQ-case only and co-morbid) and the four case categories (i.e. including being well) at stage 3 was measured by an odds ratio. Twelve odds ratios were therefore calculated comparing each clinical caseness category at stage 2 as a risk factor (compared with being well as the 'non-exposed' group) for belonging to one of four case categories at stage 3. The number, at

https://doi.org/10.1017/S0033291799008697 Published online by Cambridge University Press

stage 3, belonging to a particular case category was divided by the number not belonging to that case category (i.e. the sum of the other case categories) to determine the odds of belonging to that case category.

RESULTS

A total of 1177 patients completed both questionnaires when they presented to their GP (stage 2). Of these patients, 791 (67·2%) had completed the questionnaire during the postal survey conducted in the previous 1 to 12 months (stage 1). Six months later 971 (82·5%) patients again completed the GHQ and FQ (stage 3). Both questionnaires, at all three time points, were completed by 697 patients.

The mean age was 33·4 (range 20–48). The mean age was 2·3 years older for those who completed both questionnaires at all three time points (32·3 *v.* 34·6 year; $t = -5{\cdot}4$; $P < 0{\cdot}001$). Seventy per cent of the sample was female. Females were more likely to complete the questionnaires at all three time points. (The sex ratio for those completing the questionnaires was 73:27, while for those not, the ratio was 67:33, $\chi^2 = 5{\cdot}5$; $P = 0{\cdot}02$.) There were no other significant differences between those whose completed the questionnaires at all three time points and those who did not. Other demographic details are reported elsewhere (Wessely *et al.* 1995).

Dimensional analysis

The mean total scores for GHQ and FQ did not differ significantly at the three time points and ranged from 25·4 to 26·6 for GHQ and from 24·3 to 25·3 for FQ respectively (Table 1).

FQ and GHQ scores correlate with each other and across time points significantly (Table 2). GHQ and FQ are highly correlated when measured at the same time point (Pearson's correlation coefficient (*r*) around 0·6); fatigue correlates with fatigue at a 6 month interval or longer (*r* around 0·4); GHQ correlates with GHQ over time similarly (*r* around 0·4–0·5); FQ and GHQ also correlate across different time points (*r* around 0·3).

Table 1. *Comparison of means*

	Total GHQ score			Total FQ score		
	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3
Mean (S.D.)	26·6 (6·8)	25·6 (6·2)	25·4 (6·5)	25·3 (4·6)	24·6 (4·6)	24·3 (4·4)

Categorical analysis

Being a case of pure fatigue compared with being well at stage 2 does not increase the risk of pure psychiatric disorder 6 months later (OR = 1·0; 95% CI 0·5–1·8). Being a case of pure psychiatric disorder as opposed to being well does not make being a case of pure fatigue more likely (OR = 0·8; 95% CI 0·4–1·5). It can be seen that fatigue does not predict psychiatric disorder at 6 months and neither does psychiatric disorder predict fatigue at 6 months (see Table 6).

Each category of case had various outcomes. Tables 3 and 4 give the case category changes over 6 months. The outcome of pure fatigue caseness is highlighted in Table 5. At stage 1, 118 (15%) of the sample of 791 were cases of non-co-morbid fatigue. By stage 2, 20 (17%) were pure fatigue cases. Sixty (51%) had become well, 31 (26%) co-morbid and 7 (6%) had lost

Table 2. *Correlations*

	Total FQ score			Total GHQ score		
	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3
Total FQ score						
Stage 1	1·00	—	—	—	—	—
Stage 2	0·49	1·00	—	—	—	—
Stage 3	0·43	0·38	1·00	—	—	—
Total GHQ score						
Stage 1	0·60	0·34	0·35	1·00	—	—
Stage 2	0·34	0·57	0·23	0·49	1·00	—
Stage 3	0·29	0·33	0·61	0·42	0·40	1·00

Table 3. *Caseness category changes between stage* 1 *and stage* 2

	Stage 2				
	Well	Fatigue only	GHQ only	Co-morbid	Total
Stage 1					
Well	243	43	32	25	343
Fatigue only	60	20	7	31	118
GHQ only	45	8	36	21	110
Co-morbid	50	37	31	102	220
Total	398	108	106	179	791

https://doi.org/10.1017/S0033291799008697 Published online by Cambridge University Press

Table 4. *Caseness category changes between stage 2 and 6 months later at stage 3*

	Stage 3				
	Well	Fatigue only	GHQ only	Co-morbid	Total
Stage 2					
Well	324	54	51	49	478
Fatigue only	46	29	13	38	126
GHQ only	64	12	27	30	133
Co-morbid	65	29	38	102	234
Total	499	124	129	219	971

their fatigue caseness and had become psychiatric cases. At stage 2, there were 126 cases of pure fatigue in the sample of 1177 (11%), of which 106 (84%) were new cases. Six months later, 46 (37%) were well, with 29 (23%) being pure fatigue cases. Thirty-eight (30%) had become co-morbid, while 13 (10%) had become pure psychiatric cases. At stage 3, there were 124 cases of pure fatigue in the sample of 971 (13%), 95 (77%) of which were new cases. With respect to fatigue, therefore, 11–15% of the sample was a case of pure fatigue at each stage of which 77 to 84% had arisen within the previous 6 months. The incident rate of new cases of pure fatigue at stages 2 and 3 was 9·0% and 9·8% respectively. Of the group of pure fatigue cases, 17–23% remained a pure case when rated at the next stage. Only six of the 697 subjects for whom complete data had been collected were pure fatigue cases at all three time points i.e. < 1% of patients were thus persistently fatigued without associated psychiatric disorder for longer than 7 months.

Table 6. *Odds ratio for predicting outcome at stage 3 (caseness category at stage 2 (6 months earlier) as risk factor ('exposed' group) – comparison with non-symptomatic (non-caseness category) patients as 'non-exposed' group at stage 2)*

Stage 2	Stage 3
F	F (OR = 2·4; CI = 1·4 – 3·9)
	P (OR = 1·0; CI = 0·5 – 1·8)
	PF (OR = 3·8; CI = 2·3 – 6·1)
	W (OR = 0·3; CI = 0·2 – 0·4)
P	F (OR = 0·8; CI = 0·4 – 1·5)
	P (OR = 2·1; CI = 1·3 – 3·6)
	PF (OR = 2·6; CI = 1·5 – 4·2)
	W (OR = 0·4; CI = 0·3 – 0·7)
PF	F (OR = 1·1; CI = 0·7 – 1·8)
	P (OR = 1·6; CI = 1·0 – 2·6)
	PF (OR = 6·8; CI = 4·6 – 10·0)
	W (OR = 0·2; CI = 0·1 – 0·3)

P, pure psychiatric disorder (non-co-morbid GHQ case); F, pure fatigue case (non-co-morbid FQ case); PF, co-morbid case (GHQ and FQ caseness; W, well (non-casesness).

DISCUSSION

Our finding of a high correlation between fatigue and psychological morbidity implies that, when symptomatic, many patients have symptoms of fatigue and psychiatric disorder. This correlation

Table 5. *Outcome of 'pure' fatigure*

Stage 1 (*N* = 791)	Stage 2 (*N* = 1177) *N* (%)	Stage 3 (*N* = 971) *N* (%)
118 F	60 W (51)	
	7 P (6)	
	20 F (17)	4 W (20)
		2 P (10)
		6 F (30)
		5 PF (25)
		(3 missing)
	31 PF (26)	
	126 F (106 new cases – 84%)	46 W (37)
		13 P (10)
		29 F (23)
		38 PF (30)
		124 F (95 new cases – 77%)

W, well (non-casesness); P, pure psychiatric disorder (non-co-morbid GHQ case); F, pure fatigue case (non-co-morbid FQ case); PF, co-morbid case (GHQ and FQ caseness).

https://doi.org/10.1017/S0033291799008697 Published online by Cambridge University Press

has been found in most studies on the relationship of fatigue and psychiatric illness, in the community, primary and tertiary care.

The finding that fatigue does not predict the subsequent onset of psychiatric disorder more than the reverse or better than being well does not support the hypothesis that fatigue is more frequently a prodrome of psychiatric morbidity than that fatigue is a result of psychiatric morbidity. In contrast, Dryman & Eaton (1991) using the ECA dataset, found that fatigue predicted the onset of depression over the following year. The odds ratios were for 2·6 for women and 6·8 for men. Wilson *et al.* (1983) found that functional symptoms, including fatigue, dizziness, flatulence, etc. were nearly 17 times more likely to be present in the 18 months before an episode of depression than in non-depressed subjects. Merikangas & Angst (1994) on the other hand, in the Zurich study, found fatigue equally likely to be a prodrome as a consequence of psychiatric disorder.

Lawrie *et al.* (1997) found the incident rate for unexplained chronic fatigue (lasting at least 6 months) to be 5% per year. After excluding the subjects with 'probable psychiatric disorder' (with high GHQ scores) the incident rate of 'pure' chronic fatigue was found to be 2% per year. These figures are comparable to our findings of 9·0–9·8% incident rate for current 'pure' fatigue arising in the previous 6 months. The incident rate of pure chronic fatigue cases (those remaining cases of pure fatigue at stage 2 and 3, 6 months apart) was 2·5%.

'Pure (non-co-morbid) fatigue' is similar to pure (non-co-morbid) neurasthenia (ICD-10, WHO, 1992), a disorder where the chief symptom is fatigue for 3 months or more in the absence of affective or anxiety disorders. Merikangas & Angst (1994), in their study of neurasthenia, found 1% prevalence, similar to our finding of nearly 1% for persistent, non-co-morbid fatigue. Looking at fatigue lasting 1 month or more, the prevalence increased to 8·1%. Those authors found that the 3-month criterion 'appeared to be excessively restrictive to represent individuals with neurasthenia in the community'. At 10 year follow-up, the Zurich study reported that 31% fulfilled criteria for pure neurasthenia, 34% to be well, 14% to be co-morbid, and 21% to have only psychiatric disorder, results similar to our findings of the 6 month outcome of fatigued patients. Both the symptoms of neurasthenia and non-co-morbid fatigue, therefore, recover in the majority of patients in a short period of time. Likewise, in primary care neurasthenia and fatigue are often co-morbid with other psychological disorder.

Limitations of study

The time between stage 1 and 2 is variable. However, subdividing stage 1 scores into different time periods did not affect the correlations or predictions to stage 2. The sample is limited to adults under age 45. Our findings cannot be generalized to older people. Our sample is not a community, but a primary care sample – only the measurements at stage 1 occurred in the community. However, in UK the filter between the community and primary care is permeable. Approximately 80% of the population attend their GP each year (McCormick *et al.* 1995). Only the measurements at stage 1 occurred in the community. The mean GHQ and FQ score did not differ significantly between stages 1 and 2, underlining the permeability of this filter.

Conclusions

Fatigue and psychiatric morbidity correlate highly with each other and across time. Most patients with persistent fatigue also have psychiatric disorder. This is consistent with the idea that fatigue and psychiatric morbidity are closely associated, at least in the primary-care setting.

The outcome of non-co-morbid fatigue caseness is unstable over time with change in the direction towards either recovery (in more than a third of the sample), or psychiatric disorder (in more than a third of the sample) over time. Less than a quarter remain cases of pure fatigue at the next rating, with about three-quarters of pure fatigue cases arising within the previous 1 to 6 months.

The finding that a constant proportion of the population is symptomatic reflects a constant shifting balance between onset and resolution in the majority of subjects.

We have identified a persistent, independent state of chronic fatigue, not associated with psychological morbidity, which corresponds to the category of neurasthenia (Merikangas & Angst, 1994; Hickie *et al.* 1997). It is less common than the group with both chronic fatigue and psychological disorder and does not

https://doi.org/10.1017/S0033291799008697 Published online by Cambridge University Press

predict subsequent psychiatric disorder. Nevertheless, with a prevalence of 2·5% when lasting 6 months, and just under 1% when lasting longer than 7 months, 'pure' chronic fatigue remains an important issue in primary care.

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