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The relationship of fatigue to mental and physical health in a community sample

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Abstract *Background* Previous studies have shown fatigue and depression/anxiety to be highly associated with each other. The present study seeks to differentiate between fatigue and depression/anxiety and to investigate the familiality/heritability of fatigue using sib-pairs. *Method* The GENESiS study is a questionnaire study based in the United Kingdom that includes a five-item fatigue scale and four mental health measures (GHQ-12, EPQ-N, MASQ-AA, MASQ-HPA). Fatigue data from 10,444 sibling pairs were analysed using multivariate methods and model fitting techniques to investigate the familiality/heritability of fatigue and its relationship with the other mental health measures and physical health items. *Results* Fatigue correlated highly with GHQ-12 ($r = 0.62$, $p < 0.001$). A principal components analysis of the fatigue scale and the GHQ-12 revealed one main component which correlated highly with mental health items, and a smaller second component which correlated modestly with physical health items. Fatigue showed a modest sibling correlation (0.09, $p < 0.001$), and multivariate modelling revealed evidence for familial effects on fatigue that were independent of the mental health measures. *Conclusions* Fatigue showed a strong relationship with both physical illness and mental health measures. Fatigue is modestly familial and at least part of this familial factor is not shared with mental health measures.

Key words fatigue – depression – anxiety – mental health – physical health – comorbidity

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Introduction

Fatigue is one of the most common symptoms encountered in medical practice. Nevertheless, fatigue is difficult to define and measure, not only due to its subjectivity in meaning and experience, but also because of its multi-dimensional, heterogeneous nature. As a concept, it has been rendered both as a single, discrete contingency, and as a dimensional phenomenon that exists along a continuum of severity [4]. Fatigue is a key indicator of a variety of disorders, including chronic fatigue syndrome (CFS), multiple sclerosis (MS), systemic lupus erythematosus (SLE) and a wide range of psychiatric disturbances, stress reactions and functional somatic syndromes.

As a symptom, fatigue is repeatedly associated with psychiatric disorders in studies conducted in both primary [e. g. 3, 15] and secondary [e. g. 2] care. These studies typically find high levels of comorbidity between fatigue syndromes and depression. This type of association has also been found in studies that use community-based samples. Pawlikowska et al. [18], using a sizeable community sample, demonstrated a close correlation between scores on the 12-item General Health Questionnaire (GHQ-12) [12] and on a fatigue scale [4].

Given the close association between fatigue, depression, and anxiety, the obvious question remains as to whether fatigue exists independently of these two disorders. The answer to this question has been and remains one of close contention. As already stated, fatigue tends to be highly correlated with psychiatric disorders such as depression and anxiety both in community and primary care settings, in addition neurasthenia has always been closely associated with mood disorder [e. g. 19]. However, it is also the case that, despite the high levels of comorbidity, fatigue is never fully congruent with depression or anxiety, and indeed it has been shown [5] that chronic fatigue could be separated from psychological morbidity, but not from the tendency to have somatic symptoms. Another approach to elucidate the aetiology

of fatigue involves examining the genetics of fatigue. Farmer et al. [10], using a twin study of children, derived a model where up to 76 % of the variance of fatigue could be explained by genetic factors. Hickie et al. [14] assessed the heritability of fatigue in mid to late life, and again found a strong heritable component. In the same study, he demonstrated that depression, anxiety, psychological distress and fatigue are probably determined by different underlying genetic factors, with one uniquely contributing to fatigue. Similarly, a single environmental factor that appeared to be unique to fatigue was identified. Hickie et al. [14] also showed from previous twin studies that a shared environmental component of variance was not found to be a significant factor in fatigue.

In this study, we investigated the relationship of fatigue, mental and physical health using data collected in the GENESiS project (Genetic Environmental Nature of Emotional States in Siblings).

Subjects and methods

Recruitment and sample structure

Subjects were recruited from 26 General Practices registered with the Medical Research Council's (MRC) General Practice Research Framework (GPRF). The participating general practitioners (GPs) provided the names and addresses of all individuals registered with their practices aged between 20 and 55 years, excluding those with severe learning difficulties or psychotic illness. Subjects were sent a questionnaire, which included the five-item fatigue scale, the General Health Questionnaire (12-item version; GHQ-12) as a test of general mental health symptoms [12] and the short form of the neuroticism scale from the revised Eysenck Personality Questionnaire (EPQ-N) as a measure of trait anxiety [8]. Short forms of two subscales were used from the Mood and Anxiety Symptoms Questionnaire [20] to measure levels of anxious arousal (MASQ-AA) as well as high positive affect (MASQ-HPA) with a lower score on MASQ-HPA corresponding to an increasing level of depression. Those subjects who responded from the GP mailing list (index subjects) were then asked to provide contact information for their siblings (non-index subjects). Siblings who responded were aged between 20 and 80 years. One month later, non-responders (index and non-index subjects) were sent a reminder letter; a further month later, non-responders were re-contacted with a further reminder letter and questionnaire. During this process, if subjects no longer wished to take part, they were suspended from the study. The study, to date, has mailed questionnaires to a total of 125,000 subjects and received questionnaire responses from 42,000 subjects, representing a response rate of 34 %. Full questionnaire responses (i. e. at least three of the mental health scales described above had been completed) were received from 34,696 of these subjects. The sample was 60 % female, 98.5 % Caucasian and had an average age of 42.6 years (SD 10, range 20–80), and all levels of educational attainment and employment status were represented in the sample. The sample structure in terms of sibships and sib-pairs is illustrated in Table 1.

Table 1 GENESiS sample structure

Sibship size	Number of sibships	Number of sib-pairs
1	20,082	0
2	4,928	4,928
3	1,148	3,444
4	277	1,662
5	41	410
6	2	30
Total	26,478	10,474

Fatigue scale

We employed a five-item scale derived from the 14-item Chalder fatigue scale [4], which includes items measuring physical and mental fatigue and fatigability. The five items were chosen following an analysis carried out by Simon Wessely (not published) on 15,283 individuals from the community database maintained by Pawlikowska et al. [18]. The items used in the five-item scale were chosen as those with the highest alpha values and all chosen items had good internal consistency. This five-item fatigue scale was analysed with respect to mental health items and physical health items contained within the GENESiS questionnaire. In particular, the fatigue scale's relationship with mental health was examined to address the question of whether the fatigue scale measures a construct that is to some degree distinct from mental health.

The five-item fatigue scale was made up of the following questions: "Have you recently been having problems with tiredness?", "Have you been finding it difficult to find the correct word?", "Have you been starting things without difficulty but getting weak as you go on?", "Have you been needing to rest more?", "Have you found your muscles hurt at rest?". Responses to the items were on a four-point scale ranging from "not at all" [1] to "much more than usual" [4]. The scores on these five items were then summed and a scale ranging from 5 to 20 was constructed.

Other measures

The GENESiS questionnaire also asked subjects about the frequency of their GP consultation: "In the last 12 months, how many times have you seen your doctor?", and subjects chose a response from: 0–1, 2–4, 5–9, 10 times or more. Subjects were then asked whether they were suffering from a long-standing illness, or disability. Having answered "yes" to this question, subjects were asked about specific illnesses and asked to indicate whether they had any of the following illnesses: heart problems, breathing problems, back problems, skin disease, gut/stomach problems, diabetes, mental health problems, deafness/blindness, arthritis/rheumatism, and blood pressure problems. The questionnaire also asked about subjects' own self-perception of health: "When you compare yourself with other people of your age, do you think that you are more healthy, as healthy, slightly less healthy, or much less healthy?".

Descriptive analyses

A series of descriptive analyses were carried out on 26,478 unrelated subjects taken from the sample of 34,696 subjects. This "unrelated subjects" data set was obtained by including all individuals who had no sibling taking part in the study and also by randomly selecting an individual from each of the remaining sibships of size 2 or greater. The unrelated subjects sample was 61.5 % female with an average age of 42.4 (SD 9.9). The fatigue scale properties were examined using Cronbach's alpha and principal components analysis. The relationship of the fatigue scale to the EPQ-N, GHQ-12, MASQ-AA, MASQ-HPA and physical items was analysed using correlation analyses, t-tests and ANOVA in the software package STATA 8.0 (Statistics/Data Analysis).

Biometrical genetic analyses

A subsample of 6,394 families of maximum size 5 (equivalent to 10,444 sibling pairs, see Table 1) were used to examine the contribution of familial (genetic and shared environmental) factors to fatigue, and the extent to which these familial factors are shared with those for mental health measures.

The variance of any trait is believed to consist of three main com-

ponents; a genetic component, a shared environmental component, and a unique environmental component. It is possible to use pairs of individuals whose degree of genetic relatedness is known in order to tease apart these three components of variance. When considering twins, classical twin methodology assumes that monozygotic (identical) and dizygotic (non-identical) twins have different degrees of genetic relatedness, but identical degrees of shared environment and non-shared environment, and so the relative correlations from these two types of twins can be used to estimate a genetic component of variance. This then allows shared and non-shared environmental components of variance to be calculated. When only regular siblings are available, because all sib-pairs will share half their genes, the genetic component of variance cannot be differentiated from the shared environmental component. However, an estimate of familiality and even heritability (assuming negligible shared environment) can be estimated.

Significant sibling correlations, i. e. the degree of similarity between siblings for a trait, are assumed to result from ordinary siblings sharing half their genes and having a shared environment. So, a sibling correlation can be considered to be made up of 50 % genes and a shared environment. If one has reason to believe that the trait of interest has a minimal shared environmental component, then an estimate of heritability from a sibling correlation using Falconer's formula [9] is simply twice the sibling correlation, i. e. 2x(50 % genes). However, if this assumption of a negligible shared environmental component turned out to be false, then that heritability estimate would be 2x(50 % genes + a shared environment), which would result in some degree of overestimation of the heritability of the trait.

Using the above assumptions, structural equation model fitting analyses can be used on raw sibling data to more formally estimate a familial component and a unique environmental component of the variance of a trait. This process involves the estimation of model parameters by minimizing a goodness-of-fit statistic between observed and predicted covariance matrices. The maximum likelihood method is used to minimize the log-likelihood function through an iterative process which continues until parameter estimates are obtained that yield the smallest discrepancies between the model and the data. In order to test whether the resulting model is a good fit compared to a perfect fitting model, i. e. a saturated model, the difference in likelihood ratio chi-square (χ^2) between the models is calculated and, if there is no statistical significant difference between the models, then the more parsimonious model can be preferred. Thus, in the context of sib-pair data, the presence of a familial and/or unique environmental component can be tested and subsequently estimated. This approach can be extended to analyse the familial-environmental architecture of the covariance between the traits. Thus, the familial overlap between different disorders can be investigated.

In the present analysis, sibling correlations were calculated in order to ascertain whether familiality was present for fatigue and to also ascertain whether any familial overlap existed between fatigue and the mental health measures. Formal model fitting methods were then employed including fitting the data to a Cholesky decomposition model which allows for the pattern of covariation among different variables to be dissected into factors, the first one being common to all variables, the second being common to all except the first variable, the third being common to all except the first two variables and so on until a specific factor loads onto the last variable alone. The matrices of factor loadings reveal then the presence of factors common and/or independent to the traits analysed. A further advantage in using the Cholesky decomposition model is that it readily estimates the familial correlations among the variables.

Results

Scale analyses

The five-item fatigue scale showed a mean of 11.1 (SD 1.9), with a possible range of 5 to 20 and a Cronbach's Alpha reliability co-efficient of 0.72. A principal components analysis suggested a one-dimensional solution, with the first principal component accounting for 47.7 % of the variance.

Descriptive analyses

The fatigue scale showed a sex difference ($t = -11.7$, $df = 25434$, $p < 0.0001$) with females scoring significantly higher than males, 11.2 (95 % CI = 11.16, 11.23) compared to 10.9 (95 % CI = 10.87, 10.94). A two-way analysis of variance with age group (20–29, 30–39, 40–49, 50–59, 60+) and sex revealed that there were no significant differences between age groups; however, a significant interaction term ($F = 3.1$, $df = 4, 25431$, $p < 0.05$) resulted from younger women scoring particularly highly compared to younger men, and the difference in fatigue levels between the sexes decreased in older age groups. These findings compare favourably to previous population studies [6, 16].

Fatigue and physical health analyses

Fatigue score varied significantly according to consultation frequency ($F = 681.7$, $df = 3, 25224$, $p < 0.0001$). Bonferroni post-hoc tests showed that individuals who see their GP more often scored significantly higher on the fatigue scale. Subjects who had indicated that they were suffering from an illness scored significantly higher on the fatigue scale ($t = 27.1$; $df = 24742$, $p < 0.0001$). Fig. 1 shows mean fatigue score by illness. A regression analysis of the fatigue scale on these 11 binary illness measures revealed that all illnesses apart from deafness were significantly associated ($p < 0.0001$) with the fatigue scale; however, mental health problems, gut problems and arthritis were most predictive of high fatigue levels. The responses to the self-perception of health item were also strongly associated with the fatigue scale ($F = 316.3$, $df = 3, 6884$, $p < 0.0001$) with subjects reporting higher levels of fatigue with decreasing self-perceptions of health.

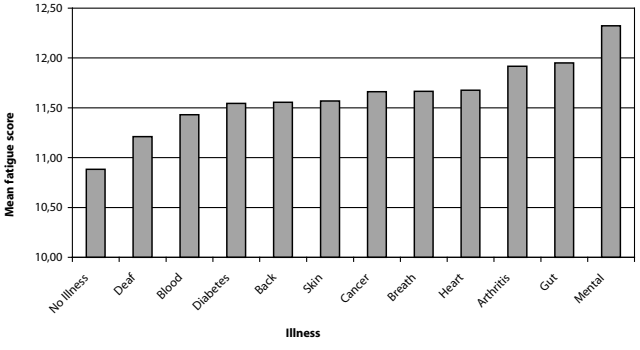

Fig. 1 Mean fatigue score by illness (*Heart* Heart Problems; *Breath* Breathing Problems; *Back* Back Problems; *Skin* Skin disease; *Gut* Gut/Stomach Problems; *Diabetes* Diabetes; *Cancer* Cancer; *Mental* Mental Health; *Deaf* Deafness/Blindness; *Arthritis* Arthritis/Rheumatism, *Blood* Blood Pressure)

Fatigue and mental health measures

The fatigue measure showed significant ($p < 0.0001$) positive correlations ranging from 0.4 to 0.6 with all anxiety- and depression-related measures (see Table 2). The largest correlation was observed between the fatigue scale and the GHQ-12 ($r = 0.62$, 95 % CI 0.61–0.63), compared to Pawlikowska's [18] findings with the full Chalder fatigue scale and GHQ-12 ($r = 0.62$, 95 % CI 0.61–0.63).

A principal components analysis was performed using items from both the fatigue and GHQ-12 scales in order to try to differentiate between the scales on a component level. The analysis suggested a two-dimensional solution, with the first principal component accounting for 43 % of the variance and the remaining principal components explaining from 8 % to 1.5 %. The first two principal components, therefore accounted for 51 % of the variance. After rotation, the GHQ-12 items loaded highly onto factor 1, while the fatigue items loaded highly onto factor 2 (see Table 3). Having generated factor scores for factor 1 and factor 2, partial correlations were calculated controlling for age and sex with the 11 binary illnesses (see Fig. 2). It can be seen clearly that factor 2 is a factor broadly associated with all the physical disorders and factor 1 a more specific factor associated with mental disorders.

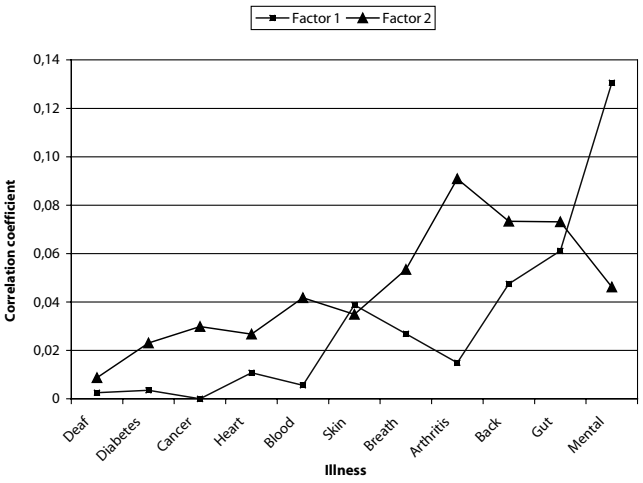

Fig. 2 Factor score partial correlations (controlling for age and sex) with binary illnesses (*Heart* Heart Problems; *Breath* Breathing Problems; *Back* Back Problems; *Skin* Skin disease; *Gut* Gut/Stomach Problems; *Diabetes* Diabetes; *Cancer* Cancer; *Mental* Mental Health; *Deaf* Deafness/Blindness; *Arthritis* Arthritis/Rheumatism, *Blood* Blood Pressure)

Table 2 Phenotypic and sibling correlations (95 % confidence intervals) for mental health measures and fatigue

Sibling / Phenotypic	Sibling 1					
	Fatigue	GHQ-12	EPQ-N	MASQ-AA	MASQ-HPA	
	0.09 (0.07 to 0.10)	0.11 (0.09 to 0.12)	0.19 (0.18 to 0.2)	0.15 (0.13 to 0.16)	0.15 (0.14 to 0.17)	
	Fatigue	0.08 (0.07 to 0.10)	0.08 (0.07 to 0.10)	0.09 (0.07 to 0.10)	−0.07 (−0.85 to −0.06)	
GHQ-12	0.62 (0.62 to 0.63)	GHQ-12	0.11 (0.10 to 0.13)	0.10 (0.08 to 0.11)	−0.10 (−0.12 to −0.10)	Sibling 2
EPQ-N	0.37 (0.36 to 0.38)	0.55 (0.54 to 0.55)	EPQ-N	0.10 (0.09 to 0.12)	−0.12 (−0.13 to −0.11)	
MASQ-AA	0.48 (0.47 to 0.48)	0.47 (0.46 to 0.48)	0.45 (0.44 to 0.46)	MASQ-AA	−0.08 (−0.10 to −0.10)	
MASQ-HPA	−0.39 (−0.41 to −0.38)	−0.59 (−0.60 to −0.58)	−0.52 (−0.53 to −0.51)	−0.33 (−0.34 to −0.32)	MASQ-HPA	

Table 3 Principal components analysis results using the fatigue scale and the GHQ-12 scale (Loadings greater than 0.5 in **bold**)

Item	Description	Factor loadings 1	Factor loadings 2
Fatigue01	Problems with tiredness	0.31	**0.70**
Fatigue02	Difficult to find correct word	0.14	0.37
Fatigue03	Starting without difficulty but getting weak	0.15	**0.59**
Fatigue04	Needing more rest	0.22	**0.75**
Fatigue05	Muscles hurt at rest	0.11	**0.62**
GHQ01	Been able to concentrate	0.33	0.39
GHQ02	Lost much sleep	**0.69**	0.27
GHQ03	Playing a useful part	0.26	0.06
GHQ04	Capable of making decisions	0.22	0.21
GHQ05	Constantly under strain	**0.71**	0.35
GHQ06	Couldn't overcome difficulties	**0.73**	0.17
GHQ07	Enjoy day-to-day activities	0.37	0.42
GHQ08	Able to face problems	0.43	0.19
GHQ09	Unhappy and depressed	**0.79**	0.19
GHQ10	Losing confidence	**0.73**	0.12
GHQ11	Worthless person	**0.67**	0.05
GHQ12	Reasonably happy	**0.56**	0.14

Sibling correlations

The sibling correlation (n = 10,444 sib-pairs) for fatigue was modest (r = 0.09, p < 0.0001), being similar for different sibship types (i. e. brothers, sisters, opposite sex), and similar to the sibling correlation for GHQ-12 (r = 0.11, p < 0.0001). These correlations assuming minimal shared environment translate to broad heritability estimates of 18 % and 22 %, respectively.

There were significant cross-trait sibling correlations between fatigue and other anxiety- and depression-related measures (see Table 2), suggesting a degree of overlap of the familial aetiological factors influencing these measures and fatigue.

Model fitting

In order to formally investigate the familiality/heritability of fatigue as well as the overlap of fatigue with respect to mental health, multivariate genetic model fitting was carried out on 6,394 families of maximum size 5. A saturated model followed by three classical multivariate genetic models (Cholesky Decomposition, Independent Pathway, Common Pathway) were fitted to the mental health variables, i. e. GHQ-12, EPQ-N, MASQ-HPA, and MASQ-AA and the fatigue variable using the raw sibship data. The difference in –2 Log-Likelihood (–2LL) between the nested model and the saturated model was examined using a chi-square test and, if a significant deterioration in fit was observed, then that model was rejected. The results of the model fitting are illustrated in Table 4.

The Independent and Common Pathway models were found to be significantly worse fits to the data than the saturated model and were, therefore, rejected. The Cholesky model illustrated in Fig. 3 was found to fit the data as well as the saturated model (–2LL = 317.2, df = 295, p = 0.18), and was, therefore, accepted as a more parsimonious fit of the data.

Under this model, which assumes shared environmental influences to be minimal, the familial components of fatigue and GHQ-12 were found to be of the order of 17 % and 21 %, respectively (very similar to the broad heritability estimates obtained from the sibling correlations). Furthermore, there were substantial familial and somewhat lower environmental correlations for the five scales (see Table 4).

In order to ascertain whether there were any specific familial effects acting upon fatigue, the coefficient for

Table 4 Fit indices from fitting multivariate genetic models to fatigue and mental health measures

Models	–2LL	df	Difference in –2LL	Difference in df	P-value
Saturated	379977	70140			
Cholesky	380294	70435	317.224	295	0.18
Independent	381136	70445	1158.797	305	< 0.0001
Common	381914	70448	1937.249	308	< 0.0001

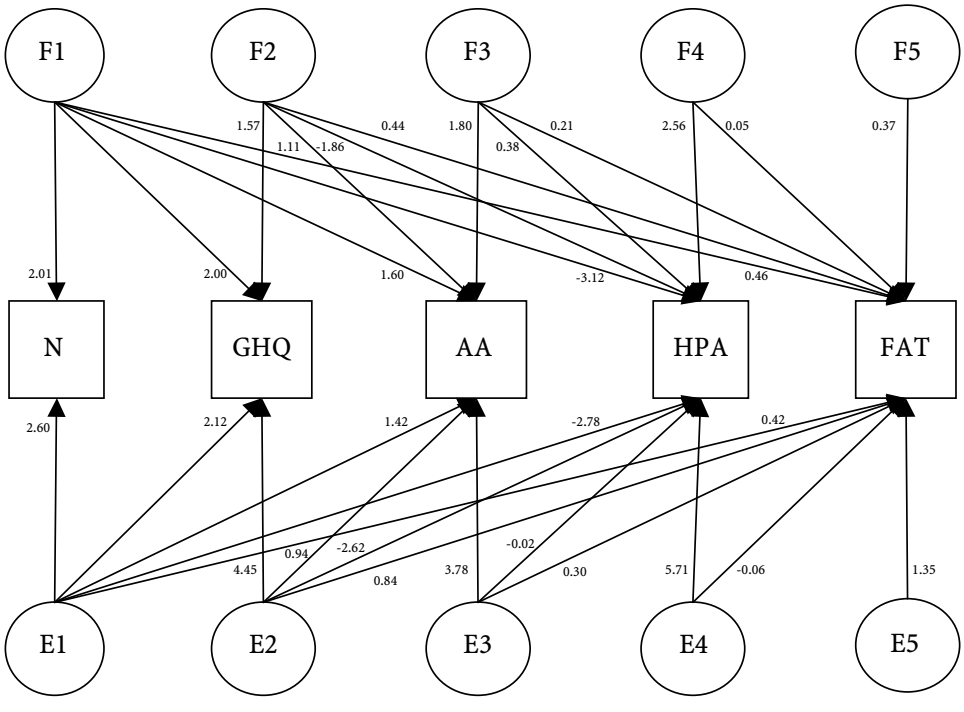

Fig. 3 Path diagram of the Cholesky Decomposition Model for mental health measures and fatigue (*F* Familial; *N* EPQ-N; *GHQ* GHQ-12; *AA* MASQ-AA; *HPA* MASQ-HPA; *FAT* Fatigue; *E* Environmental)

Table 5 Familial and environmental correlations between fatigue and mental health measures and familial and environmental proportions of phenotypic correlations between fatigue and mental health measures

	Familial correlation	Environmental correlation	Phenotypic correlation	% Familial	% Environmental
GHQ-12	0.83	0.56	0.62	26	74
EPQ-N	0.61	0.25	0.36	46	54
MASQ-AA	0.79	0.36	0.47	39	61
MASQ-HPA	−0.60	−0.32	−0.39	36	64

the specific familial path to fatigue (illustrated in Fig. 3) was fixed to zero and the resulting model was tested with respect to the full Cholesky model. A significant reduction in fit ($-2LL = 8.09$, $df = 1$, $p = 0.004$) was observed, indicating the presence of a specific familial effect on fatigue, independent of those shared with EPQ-N, GHQ-12, MASQ-AA and MASQ-HPA. In order to calculate the size of the specific familial effect on fatigue, the total unstandardized familial variance component for fatigue was calculated and found to be 0.58, and so approximately a quarter ($0.37^2/0.58 = 0.24$) of the familial effects upon fatigue were found to be specific to fatigue.

Discussion

The GENESiS five-item fatigue measure was associated with demographic and health-related variables similar to those of longer fatigue scales. It showed a strong relationship with both physical illness and mental health measures. There is also evidence to suggest that the five-item fatigue scale measures an entity that is to some degree exclusive from and also comorbid with mental health measures. In addition to this, further evidence indicates that pure fatigue is a construct with a degree of heritability.

Consistent with previous studies [e. g. 16], fatigue was more prevalent in females; no significant variation in fatigue levels was found with respect to age; and higher levels of fatigue were exhibited by individuals suffering from physical health problems. The scale also exhibited a high degree of comorbidity with the mental health measures, with a high association with the GHQ-12 scale as observed in previous work [18]. Further analyses using multivariate model fitting revealed a high degree of overlap between familial factors that influenced both fatigue and mental health measures.

The main aim of the present study was to investigate whether the fatigue scale measures a construct that is to some degree distinct from mental health measures. The principal components analysis of fatigue and GHQ-12 indicated two distinct factors that distinguished the scales from each other. The fatigue scale was found to be highly associated with a smaller factor that correlated more with physical illness. The multivariate modelling also revealed a source of familial variance on fatigue that was independent of the mental health measures. These findings together suggest that the fatigue scale, whilst being able to measure a broad psychiatric disorder construct, also measures a smaller specific construct unrelated to psychiatric disorder.

Linking this finding into research on fatigue syndromes and, in particular, chronic fatigue syndrome (CFS), the concordance between CFS and psychiatric disorder has been widely documented. However, it has also been observed that a persistent, independent state of chronic fatigue, that could be termed as 'pure' chronic fatigue, has been identified that is not associated with psychological morbidity, but which corresponds to the category of pure neurasthenia [13, 17]. This 'pure' type of CFS is less common than a type of CFS that involves both chronic fatigue and psychological disorder and does not 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 [21].

When considering the present research, it is important to acknowledge the representative nature of the sample. The overall response rate to the questionnaire was acceptable and two reminder mailings had been carried out to increase the response rate. Non-responder bias is a cause for concern in any questionnaire-based study [11]; however, in the present sample, although there was a slight preponderance of females (60 %), a trend which has been found in similar studies [e. g. 7], all socio-demographic characteristics were well represented in the sample and descriptive results for fatigue were found to be very comparable with another community-based sample [18].

Another important limitation to acknowledge is that the relative contribution of familial/heritable and environmental risk factors to the variance of a disorder in populations is not fixed. Most conditions are likely to involve gene-environment interactions, and heritability depends critically on the prevalence of environmental risk factors. Paradoxically, the more prevalent such risk factors are, the more genetic the condition will appear to be [1]. The fraction is a limited parameter that applies only to the specific population under study. Nevertheless, the present population is relatively large and also community-based, which means that the familiality/heritability results are likely to be more valid to extrapolate to the general population than, say, a clinical sample.

In conclusion, there is an increasing need for integrative research into fatigue. It would appear that, on the one hand, fatigue is very closely related to depression

and anxiety; however, on the other hand, there is also evidence for an independent fatigue syndrome in the community. If anything is clear, it is that fatigue and its syndromes cannot be understood via a single mechanism.

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References

1. Allison DB, Faith MS (1997) A proposed heuristic for communicating heritability estimates to the general public, with obesity as an example. Behav Genet 27:441–445
2. Buchwald A, Rudick-David D (1993) The symptoms of major depression. J Abnorm Psychol 102:197–205
3. Cathebras P, Robbin J, Kirmayer L, Hayton B (1992) Fatigue in primary care: prevalence, psychiatric comorbidity, illness behaviour and outcome. J Gen Intern Med 7:276–286
4. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, Wallace EP (1993) Development of a fatigue scale. J Psychosom Res 37:147–153
5. Cope H, Mann A, Pelosi A, David A (1996) Psychosocial risk factors for chronic fatigue and chronic fatigue syndrome following presumed viral infection: a case control study. Psychol Med 26: 1197–1209
6. Cox B, Blaxter M, Buckle A (1987) The Health and Lifestyle Survey. Health Promotion Research Trust, London
7. Croft P, Ridby A, Boswell R, Schollum J, Silman A (1993) The prevalence of chronic widespread pain in the general population. J Rheumatol 20:710–713
8. Eysenck SB, Eysenck HJ, Barrett P (1985) A revised version of the Psychoticism scale. Personality & Individual Differences 6:21–29
9. Falconer DS (1981) Introduction to quantitative genetics. Longman, Harlow, Essex
10. Farmer A, Scourfield J, Martin N, Cardno A, McGuæn P (1999) Is disabling fatigue in childhood influenced by genes? Psychol Med 29:279–282
11. Foster K (1998) Evaluating Non-response on Household Surveys. Office for National Statistics, London
12. Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinelli M, Gureje O, Rutter C (1997) The validity of two versions of the GHQ in the WHO study of mental illness in general health care. Psychol Med 27:191–197
13. Hickie I, Hadzi-Pavlonic D, Ricci C (1997) Reviving the diagnosis of neurasthenia. Psychol Med 27:989–994
14. Hickie I, Kirk K, Martin N (1999) Unique genetic and environmental determinants of prolonged fatigue: a twin study. Psychol Med 29:259–268
15. McDonald E, David A, Pelosi A, Mann A (1993) Chronic fatigue in general practice attenders. Psychol Med 23:987–998
16. Meltzer H, Gill D, Petticrew M, Hinds K (1995) The Prevalence of Psychiatric Morbidity among Adults Living in Private Households. HMSO, London
17. Merikangas K, Angst J (1994) Neurasthenia in a longitudinal cohort study of young adults. Psychol Med 24:1013–1024
18. Pawlikowska T, Chalder T, Hirsch SR, Wallace P, Wright DJM, Wessley SC (1994) Population based study of fatigue and psychological distress. Br Med J 308:763–766
19. Persson L, Sjoberg L (1987) Mood and Somatic Symptoms. J Psychosom Res 31:499–511
20. Watson D, Weber K, Assenheimer JS, Clark LA, Strauss ME, McCormick RA (1995) Testing a tripartite model: I. Evaluating the convergent and discriminant validity of anxiety and depression symptom scales. J Abnorm Psychol 104:3–14
21. Wessely S, Chalder T, Hirsch SR, Wallace P, Wright D (1997) The prevalence and morbidity of chronic fatigue and chronic fatigue syndrome: a prospective primary care study. Am J Public Health 87:1449–1455