Genetic and environmental contributions to the overlap between psychological, fatigue and somatic symptoms: a twin study in Sri Lanka

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Abstract

Background—Somatic symptoms often co-occur with psychological symptoms but this overlap is poorly understood. Some aspects of this overlap differ in the South Asian context, but it is not clear whether this is a reporting effect or an underlying difference in experienced illness.

Methods—Home interviews were administered to 4,024 twins randomly selected from a population-based twin register in the Colombo district of Sri Lanka (the CoTASS study). These included assessments of psychological, somatic and fatigue symptoms. The data were analysed using factor analytic and quantitative genetic approaches.

Results—Confirmatory factor analysis showed that the symptoms from the three scales represented three separate dimensions, rather than all tapping into a single dimension. However, familial correlations among the data were most consistent with a common pathway model. This implies that a portion of the underlying vulnerability is common across psychological, fatigue and somatic symptoms. There were sex differences in the aetiology of this model, with shared environmental and genetic influences playing different roles in men and women.

Conclusions—There is a complex aetiological relationship between psychological, fatigue and somatic symptoms. This is similar in Sri Lanka to Western countries, but there may be a greater influence from the family environment, suggesting that care needs to be taken when generalising research findings between countries. People who complain of certain fatigue or somatic symptoms may well also have psychologicial symptoms, or may have genetic or environmental vulnerabilities to such problems.

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Keywords

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Psychiatric disorders are associated with both somatic symptoms and functional somatic syndromes (Simon and von Korff, 1991; Henningsen *et al.* 2003). This overlap is poorly understood, but it is almost certainly bidirectional (Hotopf *et al.* 1998). One way to disentangle the aetiology of the overlap is by using genetically sensitive study designs which may indicate whether the associations can be explained by shared genes or environments. Previous family and twin studies have assessed normal variation in symptom counts to examine the overlap between fatigue and mental health (Williamson *et al.* 2005), and somatic distress and mental health (Gillespie *et al.* 2000). These studies found considerable differentiation between the risk factors for the different sorts of symptoms, yet with a strong overlap in their presentation, and a strong familial/genetic contribution to this overlap. The existence of this overlap is consistent with co-occurrence within a broader 'internalising' spectrum of symptoms, with a strong genetic contribution to the co-occurrence (Kendler *et al.* 2003). Within-person co-occurrence suggests that somatic distress also fits into this spectrum (Krueger *et al.* 2003).

Research into the relationship between somatic and psychological symptoms has been focused on populations in high income countries, but it is important to widen this focus, firstly because this relationship is well recognised in developing countries (Sumathipala, 1990; Sumathipala *et al.* 2008a; Sumathipala *et al.* 2008b). Secondly, cultural differences have been reported, including more somatic presentations in South Asia; but when both somatic and psychological symptoms are directly probed, the excess of somatic symptoms disappears (Simon *et al.* 1996; Minhas & Nizami, 2006; Simon *et al.* 1999). Thus some of the excess somatic presentations may be the result of greater acceptability of reporting of somatic symptoms, or viewing them as a 'ticket to admission' to primary care (Simon *et al.* 1999), rather than representing differences in the underlying disorders. Thirdly, if much of the high burden of somatic symptoms in developing countries is related to functional somatic or psychiatric problems, then health policies which take somatic symptoms at face value risk over-medicalising distress (Patel *et al.* 2005). Finally, investigating the aetiology of this relationship in different geographical and cultural contexts may improve understanding of the processes at work both locally but also worldwide. For example, socioeconomic, cultural, and psychosocial contexts, as well as differences in climate and ecology, may all influence the magnitude of environmental contributions identified in a twin design.

Past research using the current large population-based twin study has suggested that environmental influences on depressive disorders may be particularly strong for men in Sri Lanka (Ball *et al.* 2009; Ball *et al.* 2010a). However, the aetiology of abnormal fatigue appeared similar to previous reports from Western countries (Ball *et al.* 2010b). The present study takes a dimensional approach to the co-occurrence of psychological, fatigue and somatic symptoms over a one-month period. The main aim is to compare findings with higher-income, Western countries, and with results from studies in which diagnostic (categorical) rather than dimensional approaches have been used. The main research question is: to what extent do fatigue and somatic symptoms exist independently of one another and of psychological distress, in terms of presentation and underlying aetiology?

Methods

The study received approvals from the Institute of Psychiatry, King's College London Research Ethics Committee; the Ethical Review Committee, University of Sri Jayewardanepura; and the World Health Organisation's Research Ethics Committee.

Study design and participants

This was a population based twin study, the twin component of the **Co**lombo **T**win **A**nd **S**ingleton **S**tudy (CoTASS). Full details of the design and implementation of the study are described elsewhere (Siribaddana *et al.* 2008). Briefly, the study took place in the Colombo District of Sri Lanka, an area with population of 2.2M which includes the island's capital, and varies from urban to semi-urban areas. We added a question to the update of the annual census, asking whether the householder knew of any twins, and identified 19,302 individual twins by this method. Of these, we randomly selected 4,387 individual twins who were at least 15 years old, and spoke sufficient Sinhala to understand the interview, to take part in the project on common mental disorders. Four thousand and twenty four (91.7%) participated, including 1,954 complete twin pairs. Some preliminary analysis also used data from 2,018 singletons, who were matched to the same local area from which the twins came (Siribaddana *et al.* 2008) (singleton participation rate = 87.4%). Specially trained research workers visited the subjects' homes to interview them each separately. Interviews and questionnaires were translated in a process that aimed to retain the concepts of interest rather than a literal translation. Each component was translated at least twice independently, reviewed by a group of relevant professionals, and then by a scholar in Sinhala. Then they were trialled on lay volunteers to ensure meaning was understood (Siribaddana *et al.* 2008).

Interviews took place between 2006 and 2007, when Sri Lanka had been experiencing violent civil war for over 20 years. However, much of the conflict has centred in areas to the North and East of the island, far from the location of the current study. Nonetheless, a small minority (2.6%) of the participants reported directly participating in the conflict as combatants.

Measures

All participants were assessed on the Chalder Fatigue Questionnaire (Chalder *et al.* 1993) (CFQ). This includes 11 items assessing fatigue, and 2 assessing muscle pain, experienced over the past month (each coded 0-3).

The Bradford Somatic Inventory (Mumford *et al.* 1991a) (BSI) was developed using UK and Pakistani populations, by noting physical symptoms in the psychiatric case notes of patients with a clinical diagnosis of anxiety, depression, hysteria or hypochondriasis. From these, 21 items were selected that differentiated psychiatric from 'organic' patients (Mumford *et al.* 1991b); these include bodily aches and pains, dryness of throat, heart palpitations etc. These were each coded 0-2 based on experiences over the past month. Two of the items relate to tiredness and may thus represent item overlap with Chalder Fatigue Questionnaire; thus all analyses below were run using the 19 non-fatigue items from the BSI-21.

The Short Form 36 Health Survey questionnaire (SF36) (Ware, Jr. and Sherbourne, 1992) was also administered. It contains a set of 5 items that assess psychological aspects of mental health (such as: "Have you been a very nervous person?" and "Have you felt downhearted and blue?"). These are assessed over the past month, and were each coded 0-5.

For factor analysis, the items in each dimension were coded as described in the above paragraphs, and summed into three composite scales: *psychological symptoms* (from the 5 SF36 items), *fatigue* (from the 13 CFQ items) and *somatic symptoms* (from the 19 BSI

items). For correlations and genetic analyses, the composites were standardised within sex (to remove sex effects on the variance), mean effects of sex and age was regressed out, and log transformation was used to correct for skew.

Zygosity was assessed using a validated questionnaire (Ooki *et al.* 1990; Sumathipala *et al.* 2000) administered to both twins.

Analyses

Descriptive analyses were performed in Stata v10.1.

Phenotypic similarity—All 37 items were used as ordinal factor indicators in a confirmatory factor analysis in Mplus, using one twin randomly selected from each twin pair. The WLSMV estimator was used (weighted least-squares with mean and variance adjustment). The 37 items from all three dimensions were entered together in order to examine whether a single factor best explained the correlations between items (unidimensionality) or whether they did represent three separate factors (one for each of the scales). The three factor structure was tested in the confirmatory factor analysis for two reasons. Firstly because an exploratory factor analysis on the area-matched but independent sample of non-twins (i.e., singletons, N=2,018) from the CoTASS sample had supported the existence of either three or four factors. The fourth factor represented just two items on the Chalder Fatigue Scale (relating to slips of the tongue and finding the correct word), which is too few to reliably index an additional factor. Secondly, the three questionnaires were constructed to probe different characteristics, and retaining them as closely as possible to the originals will enhance comparability with other research.

Genetic analyses—The variances of the scales were decomposed into genetic and environmental components, by means of structural equation modelling, treating the data as continuous. Raw data analysis was used in order to include twins with missing data. These models work on the basis that monozygotic (MZ) twins share all of their additive genetic influences (A) whereas dizygotic (DZ) twins on average share only half, relative to the whole population. The environmental influences are split into those shared by members of a twin pair (C) and unique to each twin in a pair (E). Multivariate models additionally estimate the A, C and E contributions to the covariance, *e.g.*, to what extent the phenotypic overlap between psychological distress, fatigue and somatic symptoms is due to genes that influence all three. These models are based on comparisons across zygosity: where a within-trait cross-twin correlation is greater for MZ than DZ twins, we infer that genetic factors influence some of the variance in that trait; where the cross-twin cross-trait correlation (*e.g.* psychological distress in twin 1 correlated with somatic symptoms in twin 2) is greater in MZs than DZs, this indicates a genetic influence on the covariance between traits.

First a phenotypic saturated model was run, which simply estimates the phenotypic correlations without imposing a model structure. This was followed by three classical multivariate genetic models: the Cholesky decomposition, common pathway and independent pathway models (Neale & Maes, 2003). In the Cholesky model, there are three genetic factors, one of which accounts for all the genetic variance on the first variable, but is also allowed to influence the other two variables; the second genetic factor accounts for the remainder of the genetic influence on the second variable, and is also allowed to load onto the final variable; the final genetic factor accounts for the remainder of genetic influence on the final variable. There are corresponding factors for C and E influences. When including data from opposite-sex twin pairs, certain parameters must be constrained such that the correlation structure between latent factors is the same for men and women (although the

loadings of the latent factors onto measured variables are allowed to differ), and so that the order of the variables does not influence the fit of the model (Neale *et al.* 2006).

The common pathway model assumes one common latent factor that loads on to each of the three observed variables. There are A, C and E paths to the common factor, and specific (residual) A, C and E paths to each of the three observed variables. The common latent variable is constrained to have a variance of 1. The independent pathway model has a common A factor, a common C factor and a common E factor, which can independently influence all three measured variables; there are also specific (residual) A, C and E factors for each measured variable. A key difference is that the independent pathway model allows different aetiological components of common vulnerability to be unrelated to one another, whereas the convergence of the common aetiological factors through the common pathway model suggests a pre-symptomatic state of vulnerability to all three measured variables. The common pathway model might thus provide support for seeing the three measured variables as indices of 'common distress disorders' that result from vulnerability to a higher-order general internalising factor (Henningsen *et al.* 2003).

The three genetic models are each nested within the saturated model, so a χ^2 difference test can be used to assess the fit of these three models to the saturated model. The common pathway and independent pathway models are not nested within the Cholesky model, due to the constraints placed on the Cholesky model to make it appropriate for use with opposite-sex pairs. Therefore these models were compared using the Akaike Information Criterion (AIC).

In this paper we refer to 'shared' environments as the environmental influences shared within a pair of twins, and which contribute to phenotypic similarity (i.e., C); 'common' influences refer to any influences (A, C or E) that operate through the common factor (common to the three measured traits: psychological distress, fatigue and somatic symptoms).

Results

Complete data were available for 3,747 twin individuals (including 1,805 pairs of twins). The mean age was 33.9 years (range 15-85, standard deviation 13.4 years), further demographic information has been published elsewhere (Siribaddana *et al.* 2008).

Descriptive statistics

The mean summed score for psychological symptoms was 5.9 (S.E. 0.1) for men and 6.7 (0.1) for women (sex difference: t=4.60, P<0.001). This is equivalent to 76.4 (S.E. 0.4) in men, 73.3 (S.E. 0.4) in women, when using the same scoring method as a UK-based population sample, giving very similar results to this sample (Jenkinson *et al.* 1993) (among whom, men scored 74.8-78.0 and women scored 70.2 – 74.4). Note that a higher score using this scoring method indicates fewer psychological symptoms. The somatic symptoms indicated that 5% of respondents scored above the optimal cutoff for use as a screening tool to identify current psychiatric disorder (i.e., a score of 13+ using all 21 BSI items) (Mumford *et al.* 1991b); the mean score for men was 3.1 (S.E. 0.1) and for women it was 4.2 (S.E. 0.1) (sex difference: t=6.42, p<0.001). The 11 items in the Fatigue Questionnaire gave a total score of 12.3 (S.E. 0.1) for men and 12.8 (S.E. 0.1) for women (sex difference: t=5.00, P<0.001), which is very similar to the levels found in population based samples in Norway and the UK (Loge *et al.* 1998; Pawlikowska *et al.* 1994) (among whom, men scored 11.9, and women 12.6).

Correlations

The phenotypic (within-person) correlations between composite scores were, for men and women respectively, psychological distress-fatigue: 0.32 and 0.30, psychological distress-somatic: 0.28 and 0.28, fatigue-somatic: 0.51 and 0.46 (Table 1). The cross-twin correlations were higher for MZ than DZ pairs, both within-trait and cross-trait (Table 1), suggesting familial resemblance due to genetic factors, but the confidence intervals are wide. The highest MZ within-trait correlation was only 0.47, indicating a large degree of influence from nonshared environmental factors. The DZ opposite-sex (DZOS) twin pairs' correlations were not significantly different from the DZ same sex (DZSS) twin pairs', suggesting a lack of qualitative sex differences.

Confirmatory factor analysis

The 37 categorical items (5 psychological, 13 fatigue and 19 somatic) were initially all allowed to load onto a single factor. This produced a poor fit (Table 2), indicating that the items are measuring more than one underlying phenotype. Consequently, a model was run that allowed the items from the three different scales to load onto one of three factors representing each scale. This produced a good fit. The high percentage of variance accounted for, and low residual correlations, mean that composite scales of the summed items largely represent these three factors.

Genetic Models

The model fit statistics are presented in Table 3. The Cholesky, independent and common pathway models were each a good fit compared to the fully saturated phenotypic model of the data. In the Cholesky model, there was no evidence of qualitative sex differences (P>0.50), but there was a strong suggestion of quantitative sex differences ($\Delta 2ll=16.27$, df=9, P=0.061). Thus we compared the Cholesky, common pathway and independent pathway models which allowed quantitative sex differences, and selected the common pathway as the best fit on the basis of AIC (see Table 3). That is, although factor analysis indicated that the data represent three separate phenotypic factors, their aetiology can be best understood by recognising that part of their variance is explained by a common underlying vulnerability to all three sets of symptoms.

The parameters in this common pathway model could not be equated across sex (Δ-2ll =28.20, df=14, p=0.013), so we retained the model that allowed different parameters for each sex (Tables 4a and 4b, and Figure 1). In men, significant A influences came only via the latent factor; there was also a marginally significant effect of C specific to psychological distress (Δ-2ll=3.18, Δdf=1, p=0.07). This tallies with our previous finding of a possible shared environmental impact on categorically measured lifetime depressive episodes in men only (Ball *et al.* 2009). However in women, significant C influences came only via the latent factor, with additional significant A influences specific to psychological distress and somatic symptoms. In addition, there were significant E influences on the latent factor as well as specific E influences to all three measured variables in both men and women.

The latent factor had larger contributions to fatigue and somatic symptoms, accounting for 43-57% of the variance in these measured traits, but only 18% for psychological distress (Table 4B). Familial factors (A+C) were responsible for between 28% and 47% of the total variance in each trait (i.e., either directly or through the common factor), with the remainder due to nonshared environmental (E) effects. The total estimated heritability (A) for each trait was greatest for fatigue (18%) and somatic symptoms (21%) in men, and psychological (18%) and somatic symptoms (28%) in women; total C influences were greatest for psychological symptoms (23%) in men and fatigue (21%) and somatic symptoms (19%) in women. The specific E influences include measurement error specific to each trait as well as

any true nonshared environmental effects; the E that influences the common factor could include measurement error that is correlated across the three traits, as well as any true nonshared environmental influences on the common factor.

The factor loadings from the common factor to the three measured traits could be equated across sex without significant deterioration in fit (Δ-2ll=2.54, df=3, P=0.47). This shows that the common factor is tapping into the same phenotypic vulnerability in men and women, despite the differences in the aetiological influences on this common factor. When focusing on the aetiological influences on the common factor, these could not be equated across sex, regardless of whether the factor loadings had already been equated across sex (Δ-2ll=8.535 for 2df, p=0.014; or Δ-2ll=9.092 for 2df, p=0.011 after having fixed the factor loadings across sex). This demonstrates that there are sex differences specifically in the aetiology of the common vulnerability.

The models were re-run using only same-sex pairs of twins. The common pathway model was again selected as the best fitting model (using a χ^2 difference test), and the aetiological structure was very similar.

Discussion

This study finds that psychological, fatigue and somatic symptoms can be understood as relatively distinct dimensions (as shown by confirmatory factor analysis). These dimensions nonetheless share a large proportion of their genetic and environmental risk and/or protective factors (as shown through genetic model fitting assessing twin similarity). The prevalence and co-occurrence of these symptoms in Sri Lanka are similar to those in higher income, Western countries. The aetiological contributions also appear similar to those in other countries, but there are some contributions from shared environmental risk factors in this Sri Lankan context, which have not been reported in other countries.

Common vulnerability across psychological, fatigue and somatic symptoms

This is the first study in which a model with a single aetiological common factor (in addition to influences specific to each measured trait) has provided a good fit to a combination of psychological, fatigue and somatic symptoms. This suggests that comorbidity is partly the result of a prior state of vulnerability to all of these symptoms, rather than a process of phenotypic causation, as has been suggested by certain cohort studies (Harvey *et al.* 2008a; Fishbain *et al.* 1997).

Previous studies have suggested more aetiological differentiation between affective and sensory subdimensions of symptoms (Kato et al 2008; Williamson et al 2005; Gillespie et al 2000). In the current study, the common pathway explained a large proportion of the variance in all three symptom dimensions, but more so for fatigue and somatic symptoms than the psychological dimension. Nonetheless, the good fit of the common pathway model is consistent with commonly presenting psychological and physical distress being partially the outcomes of underlying core processes, which gives some justification to thinking of them as a group of 'common distress disorders' (Henningsen *et al.* 2003). It is important to note the considerable familial and nonfamilial contributions from scale-specific aetiological factors, which indicate that there is also much to differentiate these sets of symptoms.

Sex differences in familial influences on the common vulnerability

The common factor was more strongly influenced by genetic factors in men and shared (family) environmental factors in women, although nonshared environmental factors also played a large role in both men and women. This suggests there are some sex differences in the triggers for this common vulnerability to fatigue, somatic and psychological symptoms.

This is despite similar outcomes of this common vulnerability in men and women (i.e. the factor loadings contributing to psychological, somatic and fatigue symptoms were similar for men and women). The genetic contribution to the common factor is likely to represent multifactorial biological mechanisms capable of influencing affective experiences as well as somatic sensations. This could include monoamine neurotransmitter systems, as these are thought to have roles in the generation of depression as well as pain modulation, inflammatory and immune responses and neuroendocrine responses to stress (Goldenberg, 2009). While the genetic contribution to the common factor was greatest in men, and non-significant in women, a genetic role could not be ruled out in women. Additionally there were specific genetic influences on psychological distress and somatic symptoms in women, suggesting at least a small genetic role in differentiation between different but related symptom dimensions.

The finding of shared (family) environmental effects, and their different impacts for men and women, may be specific to this Sri Lankan population rather than other previously studied populations. However, it is also possible that small shared environmental influences exist in these other populations (but are typically harder to identify than genetic and nonshared environmental influences). Shared environmental effects were seen influencing both the common liability (which was more strongly related to fatigue and somatic symptoms, but also to a lesser extent to psychological distress) in women; and as a marginally significant influence specific to psychological distress in men. These effects may operate through events or exposures that occurred while still living with the family of origin such as opportunities for education, or experiences while in the marital family (which could be selected or influenced by characteristics of the family of origin, and thus exposures would be shared across twin pairs to some extent). It is unclear why these environmental influences appear to have a stronger influence on psychological symptoms in men, and fatigue and somatic symptoms in women, but this is consistent with the greater environmental influence found for men than women in this sample when using a diagnostic assessment of depression (Ball *et al.* 2009).

Links to the aetiology of medically unexplained somatic symptoms

A large proportion of physical symptoms seen in the community (Kroenke, 2003) and presenting in clinics (Nimnuan *et al.* 2001) are medically unexplained. The current study focused on symptoms known to be associated with psychiatric rather than organic disease, and the dimensional approach gave more weight to people with multiple physical symptoms (which are less likely to be medically explicable) (Nimnuan *et al.* 2001). However, there were no exclusion criteria to rule out medically explained physical symptoms. The strong pattern of familial common vulnerability across symptoms identified in our study might reflect the more population-normative end of the overlap between psychiatric disorders and functional somatic syndromes. If so, the shared environmental influences could reflect risk factors for these disorders, including illness behaviours learned from parents in childhood (Hotopf, 2002). However, parent-child similarity and childhood risk factors could also be explained by genetic influences on behaviour, *e.g.*, via perfectionist personality styles (Harvey *et al.* 2008b).

Nonshared (person-specific) environmental influences

Large nonshared environmental (E) influences were found for both men and women, and through both the common and specific paths. These might reflect the influence of stressful life events, which are known to be associated with depression (Tennant, 2002), fatigue (Kato *et al.* 2006) and other somatic problems (Tosevski & Milovancevic, 2006). But nonshared environmental influences (E) also played a large role in influencing why people experience certain symptom dimensions rather than others – these could include exposure to certain

infectious agents (Moss-Morris and Spence, 2006), or different sorts of abusive experiences (Romans *et al.* 2002). However, where assessed retrospectively, these may be subject to recall bias, and more evidence points toward psychosocial stress having a generic influence on both psychological and a range of functional somatic outcomes (Campbell *et al.* 2003). And some of these apparently environmental exposures may actually be manifestations of genetic tendencies (Tennant, 2002) that lead to common vulnerability to all three symptom dimensions.

Comparisons to other countries

One aim of research using the CoTASS sample is to assess whether aetiology differs when examined in populations living in substantially different environmental and cultural contexts to those in the majority of previous twin studies. Past studies in higher-income, Western countries found stronger support for models which place a greater emphasis on influences specific to each trait, and greater differentiation between psychological and somatic symptoms or disorders (Williamson *et al.* 2005; Kato *et al.* 2008). However, because the current study has only three measured dimensions, any differentiation between the psychological, fatigue and somatic dimensions can reside in the residual influences on the sole psychological dimension. Thus the smaller influence of the common factor on psychological distress is relatively consistent with the findings from other countries. Although the current study found a sex difference in the aetiological contributions in contrast to the above studies, the extent of the overall familial influence (A+C) was similar for men and women, and A and C can be hard to tease apart because they are correlated with one another. So, the current evidence is broadly suggestive of cross-cultural similarity, but the details are hard to compare, partly due to the small number of genetically-informative studies of this kind reported in other countries.

It is interesting that the prevalence of the symptoms measured in the current study were in line with findings from population-based studies in other countries, but the proportions of people categorised with depressive or fatigue disorders (Ball *et al.* 2010a; Ball *et al.* 2010b) was lower. This suggests that the underlying distribution of symptoms is similar across countries, but those at the high end are not well detected using diagnostic tools devised in other cultures. If so, a dimensional scale of symptoms (rather than diagnostic criteria) might provide a more level playing field from which to assess cross-cultural similarity.

Limitations

The measures we used (such as the Short Form-36 Health Survey) allowed us to tap into the variation in the general population, rather than focusing on the pathological end of the spectrum. This means the results do not directly relate to clinical conditions. However, the quantitative trait hypothesis (Plomin *et al.* 1994) postulates that aetiological risk factors influence a continuum from normal to abnormal behaviour. So understanding the influences underlying common variability may also inform us about processes that cumulatively contribute to disorders that are at the extreme end of the spectrum. Part of the reason for this approach is that the genetic models require data on large numbers of people rather than a smaller selected group. The complexity of these models still meant we had relatively little power for certain analyses, as reflected in the wide confidence intervals in tables 4a and 4b. For example, although we found no sex differences in the ACE contributions to the common factor, this may have been due to low power.

The measures we used have been designed for population-comparative purposes rather than being specific to one population. The translation procedure was very thorough and retained meaning of the relevant concepts rather than literal translation. This enabled us to have an "etic" approach, *i.e.*, examining similar phenomena in different cultural contexts. However,

this does mean the scales may have missed "emic" phenomena, *i.e.*, those understood from within the specific perspective of the population studied.

The results are based on the assumptions of the twin method, in particular the assumption that MZ twins are not treated more similarly than DZs purely because of their zygosity. Past studies have supported this assumption when examining psychiatric disorders (Kendler *et al.* 1993).

The large representative sample (the only one of its kind outside of the developed world) supports the current findings as being a valid representation for this population at this point in time. However, the results presented here do not account for potential gene-environment or gene-gene interactions within the sample, and for this reason, the results should be viewed as an overall approximation of the influences likely to be contributing.

The symptoms of all three measured dimensions come from self-reports, without any assessment to rule out physical disorders that have a medical explanation. However, the Bradford Somatic Inventory was devised to pick up symptoms that co-occur with psychiatric rather than diagnosable physical disorders. The current study contains only cross-sectional data, but genetic inheritance necessarily occurs prior to experience of psychological or physical symptoms.

Conclusion

Common underlying vulnerability predisposes to each of psychological, fatigue and somatic symptoms, although there are also risk factors specific to each. It has been suggested that somatic symptoms are especially likely to reflect (or at least co-occur with) psychological symptoms in South Asia. However, we found that the presentation and the aetiological influences (including considerable heritable contributions) on these symptoms and their overlap, are generally similar in Sri Lanka to results from higher-income, Western countries, suggesting similar underlying processes are involved.

Acknowledgments

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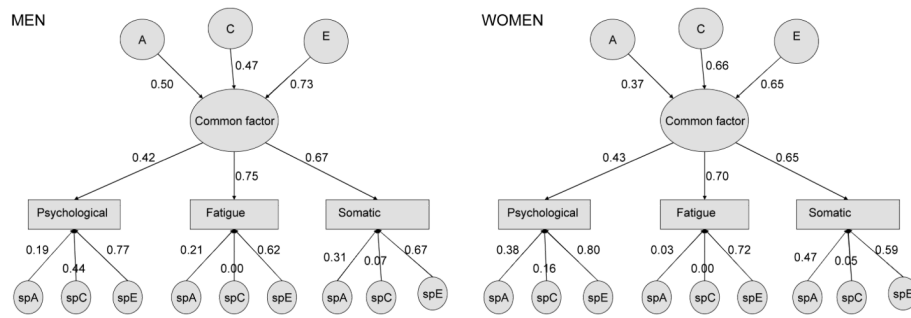
Figure 1. Common pathway model for men and women
Boxes represent measured traits. Circles represent latent (unobserved) factors that influence the measured traits. A, C and E represent influences through the common factor; spA, spC and spE represent influences specific to each of the three measured traits. Arrows represent standardized paths, which are squared to indicate the magnitude (variance) of the relevant factors shown in table 4.

Table 1

Correlations (95% CIs) between composite scores (within men and women, and between MZM, MZF, DZM, DZF and DZOS pairs)

Composite scale	Cross – twin					Within person	
	MZM	DZM	MZF	DZF	DZOS	Men	Women
Within-trait							
Psychological	0.31 (0.21-0.39)	0.24 (0.11-0.36)	0.29 (0.21-0.37)	0.15 (0.03-0.25)	0.16 (0.08-0.24)	-	-
Fatigue	0.31 (0.21-0.40)	0.20 (0.08-0.32)	0.28 (0.19-0.36)	0.20 (0.09-0.31)	0.12 (0.04-0.20)	-	-
Somatic	0.32 (0.23-0.41)	0.21 (0.09-0.33)	0.47 (0.40-0.54)	0.33 (0.24-0.42)	0.18 (0.10-0.26)	-	-
Cross-trait							
Psychological-fatigue	0.13 (0.03-0.23)	0.06 (−0.07-0.19)	0.15 (0.06-0.24)	0.07 (−0.04-0.18)	0.08 (0.00-0.15)	0.32 (0.27-0.36)	0.30 (0.26-0.34)
Psychological-somatic	0.17 (0.07-0.26)	0.01 (−0.13-0.14)	0.16 (0.08-0.24)	0.08 (−0.02-0.18)	0.08 (−0.01-0.16)	0.28 (0.23-0.32)	0.28 (0.24-0.32)
Fatigue-somatic	0.27 (0.17-0.36)	0.18 (0.06-0.30)	0.24 (0.16-0.32)	0.23 (0.14-0.32)	0.09 (0.01-0.17)	0.51 (0.47-0.54)	0.46 (0.42-0.49)

Table 2

Confirmatory factor analysis (CFA) fit of 3-factor model and 1-factor model

Model	Proportion of variance explained	Root mean square residual	Average absolute residual correlation	CFI	TLI	RMSEA
1. Unidimensional (CFA with 1 factor)	35%	0.111	0.092	0.771	0.872	0.100
2. CFA with 3 items (separating the 3 scales)	47%	0.050	0.042	0.932	0.973	0.046

Number of items: 37; number of individuals: 1,988

Table 3

Genetic model fit statistics

Model	Model fit statistics		Fit statistics (compared to phenotypic saturated model)			
	−2 ll	df	Δ −2ll	Δ df	P-value	Δ AIC
1. Phenotypic saturated	55319.66	11259	-	-	-	-
2. Cholesky	55396.51	11337	76.85	78	0.516	−79.15
3. Common pathway	**55388.18**	**11336**	**68.52**	**77**	**0.744**	**−85.48**
4. Independent pathway	55383.66	11328	64.00	69	0.648	−74.00

Bold indicates best fitting model.

All models allow separate parameter estimates according to sex

Table 4A

Common pathway model of genetic and environmental influences: Contributions to the common factor

Sex	Contributions to variance of common factor (95% CI)		
	A	C	E
Men	0.25 (0.01-0.60)	0.22 (0.00-0.43)	0.53 (0.41-0.66)
Women	0.14 (0.00-0.45)	0.44 (0.18-0.62)	0.42 (0.32-0.54)

Table 4B

Common pathway model of genetic and environmental influences: Contributions to the variance in the three measured variable

| Sex | Measured trait | Specific A | Contributions to variance (95% CI) | | | | Overall source of variance | | |
			Specific C	Specific E	Common factor		A	C	E
Men	Psychological	0.04 (0.00-0.28)	0.19 (0.00-0.28)^	0.60 (0.52-0.67)	0.18 (0.14-0.22)		0.08	0.23	0.69
	Fatigue	0.04 (0.00-0.12)	0.00 (0.00-0.09)	0.39 (0.30-0.48)	0.57 (0.48-0.67)		0.18	0.12	0.68
	Somatic	0.10 (0.00-0.17)	0.00 (0.00-0.14)	0.45 (0.37-0.53)	0.45 (0.38-0.53)		0.21	0.10	0.69
Women	Psychological	0.15 (0.02-0.24)	0.03 (0.00-0.14)	0.64 (0.57-0.72)	0.18 (0.14-0.23)		0.17	0.11	0.72
	Fatigue	0.00 (0.00-0.06)	0.00 (0.00-0.04)	0.52 (0.44-0.58)	0.48 (0.41-0.55)		0.07	0.21	0.73
	Somatic	0.22 (0.04-0.29)	0.00 (0.00-0.15)	0.35 (0.29-0.42)	0.43 (0.36-0.50)		0.28	0.19	0.53

^
Marginally significant, P=0.07