Chronic fatigue syndrome

Role of psychological factors overemphasised

EDITOR,—In concluding that psychological factors are more important than immunological ones in determining the long term outcome of myalgic encephalomyelitis or the chronic fatigue syndrome Andrew Wilson and colleagues seem overconfident of the validity of their findings.[1] Although the use of self rated measures of outcome is necessary, the validity of the investigators' treatment of such data is questionable. For example, the five point self rated global illness outcome was dichotomised such that an original response of "not improved at all" was recorded to "worsened"—a decision the investigators fail to justify. It is also dubious whether patients' recall of their own premorbid psychological state is accurate, given that the average onset was 9·2 years before recall and the finding that memory of an event is affected by subsequent events.[2]

Further, the association of "disease conviction" to lack of improved global outcome at follow up may reflect the fact that patients with severe physical symptoms (for example, inability to walk) attribute their disease to a physical basis more than do patients who experience mild symptoms (for example, headaches and tiredness). In this way disease conviction could be measuring disease severity. The possibility that self rated outcome variables may thus be invalidated suggest that caution is needed in interpretation, which the authors fail to note.

In line with the above reasoning, objective measures of outcome may be more representative of the true state of affairs, in which case results of delayed hypersensitivity skin tests and the Karnofsky performance index data (rated by one of the investigators) should receive relatively more focus. The only significant predictors of delayed hypersensitivity at follow up, however, were cutaneous energy at initial assessment, which is not surprising (and suggests that people who were more immunologically compromised at entry to the study were not likely to have improved at follow up), and the absence of a premorbid psychiatric diagnosis—a relation that is left unexplained.

As for results from multiple regressions predicting Karnofsky performance scores, the parameter estimates necessary to evaluate the contribution of individual predictor variables (that is, change in R^2 and its corresponding significance level) are not reported. Instead, results of bivariate t tests are reported, but no indication is made of whether α inflation due to repeated measures was corrected. A Bonferroni correction would result in a critical α of 0·0005, which none of the variables exceeded.

Additionally, a lot is made of the finding that 20 of the 103 patients in the study were given an alternative psychiatric diagnosis at follow up. Equally important, however, is the fact that this diagnosis was not made at the initial assessment. It might therefore be argued that psychiatric distress was a result of having a disability that did not improve rather than vice versa. This begs the question of why interaction terms were not included in the analyses. Alternatively, a relevant empirical question is whether the association of psychological factors and illness outcome would persist if this subsample was excluded from analyses.

Advice to authors

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Thus, Wilson and colleagues present a pilot analysis of the influence of psychological and immunological factors in the outcome of myalgic encephalomyelitis; but caution should have been exerted in their interpretation of the results. Only replication will tell if their conclusions are valid.

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1 Wilson A, Hickie I, Lloyd A, Hadzi-Pavlovic D, Boughton C, Dwyer J, *et al.* Longitudinal study of outcome of chronic fatigue syndrome. *BMJ* 1994;**308**:756-9. (19 March.)
2 Loftus ES, Hoffman HG. Misinformation and memory: the creation of new memories. *J Exp Psychol [Gen]* 1989;**118**: 100-4.

Authors' reply

EDITOR,—In our study design we included both self reported and more objective measures of functional status as we accept the need to use both in patients with the chronic fatigue syndrome. The strength of the belief in a solely physical disease process predicted poor long term outcomes as determined by both subjective and objective outcome measures.

Receipt of a disability benefit was not used as an outcome variable. Though it may seem to be a more robust measure than self reported instruments, it can also be confounded by various other factors such as premorbid financial status, access to alternative financial support, duration of disability, and personal attitudes towards disability payments.

The comment that patients who were immunologically compromised at entry to the trial were not likely to have improved at follow up is not correct. We reported that impaired response to skin tests at entry to the trial had no bearing on functional outcome. Also, in our discussion we specifically commented on the relation between the absence of a premorbid psychiatric diagnosis and immunological function at follow up as possible evidence for a link between psychological factors such as denial of illness and immune function.

While use of the Bonferroni correction is unusual in logistic regression, we agree that it can be used to control the type 1 error rate for a family of significance tests. This approach can be fairly conservative when there is dependency between the tests and would be conservative in the extreme under the authors' suggestion of dividing α by 100 (0·0005 = 0·05/100). The addition of more variables to examine sufficient interaction effects would not be plausible for the moderate sample size even by our more liberal approach, let alone the authors' conservative one.

We acknowledged the possibility that more severe symptoms may alter attitudes to illness, but Chris Blatch and Teeya Blatt have confused the presence of psychological distress (which may be expected to increase with severity of illness or chronicity) with the designation of an alternative psychiatric diagnosis. The consensus psychiatric diagnosis was based on all available data—notably, changes in the pattern of symptoms over time. When subjects with an alternative psychiatric diagnosis (n=20) were excluded from the regression analyses the association between physical disease conviction and outcome of illness was unchanged. Physical disease conviction remained the sole predictor of global outcome rated by the subject (P=0·02) and the Karnofsky score rated by the investigator (P=0·01).

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Distinguish between syndromes . . .

EDITOR,—I note that several people writing in the *BMJ* are still confusing myalgic encephalomyelitis with the chronic fatigue syndrome.[1] I wish to clarify matters. From a scientist's point of view, the main problem is not the term chronic fatigue syndrome but the various diagnostic criteria that go with it. For instance, the strict Australian definition adopted by Wilson *et al* is similar to that for myalgic encephalomyelitis.[2] As a result, it is reasonably certain that in this article the two names probably refer to the same disease.

The "Oxford" criteria used in Britain, however, are far broader, covering all patients whose severe, unexplained fatigue has been present for at least half of the time and for at least six months. The only other requirements are that the fatigue must have had a definite onset and that it affects both physical and mental functioning. Unlike with the strict Australian definition, no immunological criteria have to be met.[2] Moreover, there do not have to be appreciable fluctuations in symptoms—still a major criterion for myalgic encephalomyelitis.

In terms of prevalence, a recent study found that 17 of 686 (2·5%) attenders in general practice fulfilled the Oxford criteria for the chronic fatigue syndrome.[3] When a further four patients who did not meet the criterion of a definite onset were also included the estimated prevalence increased to 3%. In contrast, the prevalence of myalgic encephalomyelitis rarely exceeds 1·5 per 1000.[4]

Most patients who fulfil the Oxford criteria suffer not from myalgic encephalomyelitis but from more common conditions, notably depression, anxiety states, sleep disorders, and fibromyalgia. None of these disorders occur in epidemics, and most