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Chronic fatigue syndrome

SIR: Perhaps the most welcome feature of the paper by Hickie *et al* (*Journal*, April 1990, **156**, 534–540) is the demonstration that physicians and psychiatrists can work profitably together in studies of the still controversial chronic fatigue syndrome (CFS). In addition, the use of standardised instruments and the detailed information given on the sample represent a significant advance on much previous work (David *et al*, 1988). The authors correctly note that the selected nature of the sample limits the generalisations that can be drawn from the study, especially since only a quarter of the 200 eligible patients were actually psychiatrically assessed. However, they still make several conclusions that may not be justified.

The authors suggest that their study contradicts other findings that psychiatric diagnoses are an important feature in patients fulfilling criteria for CFS. Of their sample, 46% fulfilled criteria for major depression during the course of their illness. The figure for current depression was lower, but as 15 of the sample had already completed a treatment trial, and given the remarkable placebo response rate that others have observed in this condition (Gantz & Holmes, 1989), current status is misleading. This figure of 46% is in fact in keeping with other studies of psychopathology and CFS. We studied consecutive referrals to a neurological hospital with severe fatigue that had not been explained despite intensive medical investigation (Wessely & Powell, 1989). In terms of symptoms, these resembled the subjects reported by Dr Hickie *et al*, as nearly all complained of myalgia, paraesthesiae, memory impairment, poor concentration, etc, and 72% reported that their illness had commenced with a viral infection. A total of 47% fulfilled criteria for major depression even when fatigue was excluded as diagnostic symptom (Wessely & Powell, 1989). An identical figure was provided by Manu *et al* (1988), as well as by the two US studies cited by the authors. Only one recent study is discrepant. Millon *et al* (1989) studied CFS patients in a US allergy clinic, who might be thought comparable with those in the current paper. They did not give diagnoses, but found considerably higher scores on the Hamilton Rating Scale for Depression (with 19/24 exceeding the conventional cut-off) than those reported by Dr Hickie *et al*. Thus the findings of Dr Hickie *et al* on rates of depression are in keeping with previous studies, and confirm the importance of routinely assessing mood in chronically fatigued patients.

The other four diagnostic studies also found that an additional (approximately) 20% of subjects fulfilled criteria for other psychiatric disorders, principally anxiety and somatisation disorders. It is not the rates of depression then but the absence of other disorders that is surprising in the study of Dr Hickie *et al*. In our study, the proportion of CFS patients with *any* psychiatric disorder was 72% in total, compared with 36% of controls with fatigue due to neuromuscular disease, matched for length of illness (Wessely & Powell, 1989). That this excess of psychiatric illness in CFS may be a result of the central production of cytokines, as suggested by Dr Hickie *et al*, remains plausible but unproven.

The authors use their findings of low rates of premorbid psychiatric disorder (which does contrast with the American studies cited) to suggest that this is not a risk factor for the development of CFS. However, the design of both this and the American studies does not permit either conclusion. The patients reached the investigators by a complex series of filters, and it is reasonable to assume that general practitioners were more likely to refer patients with severe fatigue and a known psychiatric history elsewhere,

reserving an immunological assessment for those with new-onset syndromes. The different health care system in the USA, in which patients have more direct access to specialists, gives a different bias, and may have accounted for the contradictory results. It is difficult to establish the true role of past psychiatric history in the genesis of CFS using hospital-based case-control studies.

The authors do not emphasise somatisation as a significant process in CFS, partly on the results of the Illness Behaviour Questionnaire (IBQ). Given the nature of the sample, it is perhaps unwise to put much credence on the results of a questionnaire that includes such unsubtle questions as "If a disease is brought to your attention do you worry about getting it yourself?". However, the authors make one further important clinical observation. They report that the patients firmly believed in the physical nature of their condition, and rejected any psychological contribution. Such observations are in keeping with other studies of the condition (Imboden *et al*, 1959; Wesseley, 1990), emphasised by the classic quotation on neurasthenia at the start of their paper. This suggests an additional characteristic of many chronic sufferers that may be more clinically important than the presence or absence of either immunological or psychiatric disorder.

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SIR: We enjoyed the paper by Hickie *et al* (*Journal*, April 1990, **156**, 534–540), but wish to comment on the interpretation of the results.

Selection of depressed controls should avoid unintentional overlap with CFS patients. Overlap occurs in physical markers such as the VP-1 antigen (a proposed marker of chronic enterovirus infection) with groups such as major depressives (Lynch & Seth, 1989) and those with neuromuscular disorders (Halpin & Wessely, 1989). From further studies we estimate that 30–40% of our depressed controls would show other similar physical abnormalities to CFS patients (Lynch *et al*, 1990, submitted). For these reasons, depressed controls should undergo the same assessment as for CFS and patients with significant physical abnormalities should be excluded.

Secondly, the control group should be homogeneous; in this study, patients possibly with different types and severity of depression are included. We found that in-patient depressed controls had more severe depressive symptoms and fatigue than out-patients, whom CFS patients resemble more in terms of depressive and fatigue severity. We would advocate using out-patients with major depression of milder severity (Lynch & Seth, 1990).

Assessment for both control group and CFS should be initially without medication (antidepressants have quite marked effects on depression and fatigue complaints in previously untreated depressives by the second week of treatment). Other difficulties are whether fatigue should be excluded from diagnostic criteria, as its nature is uncertain in the chronic fatigue syndrome (Wessely & Powell, 1989).

The conclusion that ". . . there is no evidence that CFS is a variant or expression of a depressive disorder . . ." is not justified. The control group used was of typical major depression and findings only hold for this group and not other depressive groups. There are also alternative explanations consistent with the findings on phenomenology and illness behaviour.

Regarding phenomenology; in the analogous situation of atypical facial pain, for example, there is one major symptom of pain, and depressive symptoms may not be obvious. This group would also differ phenomenologically from the depressed controls in Dr Hickie *et al*'s study. This study design cannot in itself refute or confirm whether CFS is an atypical depressive syndrome. The findings on illness behaviour are consistent with those of Wessely & Powell (1989) and Wessely *et al* (1990) in that the differences in attribution of symptoms explain why depressive symptoms such as self-esteem and guilt are more prominent in major depression than CFS. This can be taken to support or refute the above hypothesis concerning CFS. The only certain way of resolving this dilemma is to clarify the nature of fatigue in CFS