We do not understand what the correspondents mean when they describe our patient group as "heterogeneous" since they are carefully described and come from a clearly defined epidemiological population. The role of viral illness in causing chronic fatigue remains undetermined and it is at present impossible to state with any certainty whether a patient's fatigue is a consequence of a viral infection. It was never "assumed that their symptoms might have been caused by encephalitis".

The correspondents comment that "the results of this study indicate that the subjective reports might have been exaggerated or even inaccurate". It is not clear on what evidence they are basing this opinion – if it is because few deficits were revealed on objective cognitive testing, it is precisely this discrepancy which has been noted consistently by other researchers. Goudsmit & Howes, however, suggest that we should reconsider our diagnosis of CFS subjects (of whom there were 21 not 11 as they state) post-hoc because of it. This would be scientifically invalid. Such comments also demonstrate precisely our point in exercising caution in the use and interpretation of neuropsychological tests to confirm or refute an organic basis for CFS.

The study by Riccio *et al* (1992) is commendable as being one of the first in the area. However, the authors described their results as preliminary; their nine patients with ME had significantly higher scores than controls on the depression subscale of the HAD, and 2 were defined as retarded depression using the PSE. It is now clear that studies of this kind must take into account coincident depression and anxiety in subjects with severe fatigue when assessing cognitive performance. Another advance in research in this area has been the near universal adoption of operational criteria for chronic fatigue syndrome, in preference to the potentially misleading term myalgic encephalomyelitis.

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Comorbidity and suicide risk

SIR: Hornig & McNally (1995) argue that we did not control optimally for comorbid disorders known to increase suicide risk. In our initial paper (Weissman *et al*, 1989), we controlled statistically for major depression, alcohol and drug abuse, and agoraphobia separately, and for the latter three disorders, in combination. The odds ratio did not change significantly with all of these combinations.

In a follow-up report based on the ECA data (Johnson *et al*, 1990), we directly estimated the risk of suicide attempts in individuals with uncomplicated panic disorder compared to comorbid conditions. We also conducted similar analyses for major depression. We showed that the lifetime rates of suicide attempt in individuals with uncomplicated panic disorder (7.0%) were higher that for persons with no psychiatric disorder (1.0%), giving a significant odds ratio of 5.4 with 95% CI of 1.9–15.4. (Although the numerator of this rate of suicide attempts in individuals with uncomplicated panic disorder consists of four individuals with a lifetime diagnosis of uncomplicated panic disorder who attempted suicide, the total sample size (denominator) on which this rate is based is the 57 individuals with uncomplicated panic disorder, which in our opinion is a reasonable sample size.) We also showed that the lifetime rate of suicide attempts in individuals with uncomplicated major depression was 7.9%, a figure which is clearly not significantly greater (either statistically or clinically) from that of the rate for individuals with uncomplicated panic disorder. More importantly, we showed that individuals with comorbid panic disorder have rates of suicide attempts equal to that of individuals with comorbid major depression.

Hornig & McNally have now compared the rates of suicide attempts in individuals with specified "uncomplicated" psychiatric disorders to the rates of suicide attempts in individuals with only that specified disorder and panic disorder (their Table 2). Their interpretation of their results is that "uncomplicated" panic disorder does not confer any additional risk for suicide attempts over and above that associated with the specified uncomplicated psychiatric disorder. However, one could use the data presented in their Table 2 using their same logic to argue that the presence of a psychiatric disorder, such as major depression, in addition to panic disorder does not increase the risk of suicide attempts in those with uncomplicated panic disorder. This may be done by comparing the value of 7.0% (the rate of suicide attempt in those with uncomplicated panic) to that of 0% (the rate of suicide attempt in individuals with only major depression and panic) to conclude that the presence of comorbid major depression does not increase the risk of suicide attempts in individuals over that associated with uncomplicated panic. Clearly, this implausible result, which is inconsistent with results from a number of clinical studies, is due to

the fact that these numbers are too small to be meaningful.

Hornig & McNally have also extended our methods (Weissman *et al*, 1989) to simultaneously include six psychiatric disorders other than panic disorder, in addition to the three included in that original paper. This was done in an effort to control for the confounding effects of these comorbid disorders on the association between panic disorder and suicide attempts. Their Table 1 presents the results obtained by including in the model nine psychiatric disorders in addition to panic disorder and sociodemographic variables. The results of their analyses show that the effect of panic disorder on suicide attempts is not statistically significant under these circumstances. However, when we carry their analyses a step further and include social phobia (which appears to meet the same criteria as the other nine psychiatric disorders regarding its inclusion in the model as a potential confound; Schneier *et al*, 1992), we find that the association of panic disorder with suicide attempts is indeed significant ($P<0.0145$).

We agree with Hornig & McNally that comorbid conditions strongly influence the degree to which individuals with panic disorder are at risk for suicide attempts. We especially note that estimating the strength of this association will vary with the specific comorbid variables that are included in the model as we have demonstrated here. Therefore, the direct estimate of the risk of suicide in uncomplicated panic disorder is of the most interest. These arguments as well as supporting studies are summarised by Johnson *et al* (1992).

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Five group comparisons of treatments for anxiety disorders

SIR: Oehrberg *et al*'s (1995) comparison of the SSRI paroxetine and placebo in the treatment of panic disorder and agoraphobia reports an advantage for paroxetine treated patients. Patients in this study received standardised cognitive behaviour therapy along with their primary treatment (paroxetine or placebo). This design does not, however, permit a comparison of the efficacy and tolerability of paroxetine and placebo as is claimed. For paroxetine and placebo to be compared irrespective of cognitive behaviour therapy, one would have to assume an equivalent effect for the cognitive behaviour therapy for all patients in both drug groups. The design also ignores the possibility of differential drug by cognitive behaviour therapy interactions. The study design therefore only permits a comparison of paroxetine *plus* cognitive behaviour therapy with placebo *plus* cognitive behaviour therapy. A full comparison of paroxetine, placebo and cognitive behaviour therapy, would require a minimum of *five* treatment groups (Hollon & De Rubies, 1981), namely; paroxetine alone, placebo alone, cognitive behaviour therapy alone, paroxetine plus cognitive behaviour therapy, and placebo plus cognitive behaviour therapy.

Such five group comparisons of pharmacological and psychological treatments for anxiety disorders are rare, with one published study to date, comparing diazepam, placebo, and cognitive behaviour therapy alone and in combination in the treatment of generalised anxiety disorder (Power *et al*, 1990). We have recently completed a second five group study comparing the relative and combined efficacies of the SSRI fluvoxamine, placebo and cognitive behaviour therapy in the treatment of panic disorder and agoraphobia (Sharp *et al*, in press). The results of these more comprehensive studies suggest that the design used by Oehrberg *et al* is unreliable. This is particularly so for the placebo plus cognitive behaviour therapy group. In our studies this combination was more effective than the placebo alone treatment but less effective than the cognitive behaviour therapy alone condition, and is thus an inadequate representation of either placebo or cognitive behaviour therapy used alone. Such information could only be provided by a five group comparison which is the minimum standard design for such studies.

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