

## Letter

# Stress and exacerbations in multiple sclerosis

## Whether stress triggers relapses remains a conundrum

EDITOR—The front page of the *BMJ* of 20 September 2003 carries the title: "Relapse in multiple sclerosis: stressful life events increase exacerbations." Buljevac et al present evidence that psychological stress is associated with a doubling in risk of relapse.<sup>1</sup> Two issues arise.

Firstly, this study has limitations, some of which are clearly acknowledged by the authors. The most critical limitation of the study is recall bias. Patients having a relapse are more likely to seek an explanation and hence report stressful events during preceding weeks. In other diseases such as myocardial infarction, patients commonly attribute their illnesses to psychological factors.<sup>2</sup>

Secondly, association does not equate to causality. An alternative hypothesis is that "psychological stress" and neurological relapse are different temporally disseminated manifestations of the same underlying disease process. Magnetisation transfer changes precede the traditional radiological signs accompanying clinically overt neurological relapse by up to three months.<sup>3</sup> Subclinical reversible cognitive changes accompany relapses.<sup>4</sup>



Thus an appreciable number of negative life events could have occurred, or be perceived to have occurred, as a result of subtle changes in cognition or behaviour preceding an overt clinical relapse. Several groups have reported the presence of an association between relapse and mild to moderate stressful life events (which might occur secondary to changes in daily life management). This association disappears with major negative life events (which are beyond control).<sup>5</sup> Since disease burden was not controlled for, we do not know whether stressful life events predicted relapse independently of what may have also elicited such events.

The study's impact on the understanding of relapse pathogenesis needs to be assessed with caution.

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## References

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