

LETTERS TO THE EDITOR

Creutzfeldt-Jakob disease and stress

As part of a study on risk factors for Creutzfeldt-Jakob disease, we compared frequencies of stressful life events in cases of Creutzfeldt-Jakob disease and controls. Cases were patients classified as definite or probable sporadic Creutzfeldt-Jakob disease according to the criteria of Masters *et al*¹; they were matched on sex and age (\pm five years) with non-demented hospital controls. Data on history of patients with Creutzfeldt-Jakob disease were obtained from close relatives.

The study sample consisted of 55 case-control pairs (61.8% women); mean ages were 64.0 for cases and 63.8 years for controls. In the present analysis, we focused on events which had occurred between one year and five years before the onset of disease. Overall, we found that 27 patients with Creutzfeldt-Jakob disease (49%) and four controls (7.2%) had experienced emotional disturbances due to life events (table). The proportion of major life events was significantly higher in patients with Creutzfeldt-Jakob disease than in controls (χ^2 (matched pairs) = 19.6, df = 1, $P < 0.001$).

Studies on life events are subjected to much criticism. Recall bias is the most important issue. Relatives of patients with Creutzfeldt-Jakob disease may pay more attention to the occurrence of life events than controls. However, as shown in the table, we have restricted analysis to major events. It is unlikely that relatives of patients have reported events which have not occurred and that controls have forgotten such important personal events. Differential referral of cases of Creutzfeldt-Jakob disease and hospital controls according to past life events may be another issue.

Other studies have shown that stressful life events could be risk factors for different diseases, especially cardiovascular diseases and cancer. Mechanisms of the associations have not been totally elucidated, but some plausible hypotheses have been proposed. Regarding the association between Creutzfeldt-Jakob disease and life events, different interpretations can be proposed. Stress related biological conditions might enhance the formation of abnormal prion protein. Stress might also increase the severity of subclinical symptoms. This hypothesis has been proposed to explain the early age of

onset of bovine spongiform encephalitis in animals which had been moved between herds.²

JEAN-PHILIPPE BRANDEL
NICOLE DELASNERIE-LAUPRETRE
INSERM U 360, Hôpital de la Salpêtrière

Correspondence to: Dr Jean-Philippe Brandel, INSERM U 360, Hôpital de la Salpêtrière 75651 Paris Cédex 13, France.

- 1 Masters CL, Harris JO, Gajdusek DC, Gibbs CJ, Bernoulli C, Asher DM. Patterns of worldwide occurrence and the significance of familial and sporadic clustering. *Ann Neurol* 1979;5:177-88.
- 2 Anderson RM, Donnelly CA, Ferguson NM, Woolhouse MEJ, Watt CJ, Udy HJ, *et al*. Transmission dynamics and epidemiology of BSE in British cattle. *Nature* 1996;382:779-88.

Wasting, weakness, and the MRC scale in the first dorsal interosseous muscle

The Medical Research Council (MRC) scale¹ retains its popularity as a robust clinical tool for assessing hand muscle strength. It is, however, non-linear and a change of one unit in the scale, say from 5 to 4, represents a much greater loss of muscle force than from 1 to 0. An opportunity to explore the nature of this non-linearity arose during a serial study of the first dorsal interosseous muscle in a series of 40 patients with amyotrophic lateral sclerosis. In both hands of each patient, a single observer documented the MRC scale for strength and estimated the degree of wasting of the first dorsal interosseous muscle on a four point scale (no wasting 4; mild 3; moderate 2; or severe wasting 1). Subsequently, the peak to peak amplitude of the compound muscle action potential (CMAP) evoked by supramaximal ulnar nerve stimulation at the wrist was measured. As this is a purely objective measurement, there was no biasing of the force or wasting estimates by prior knowledge of the CMAP amplitude. Patients were assessed at three month intervals with the assessor blind to the results from previous visits. The study yielded 183 observations on which to base an analysis.

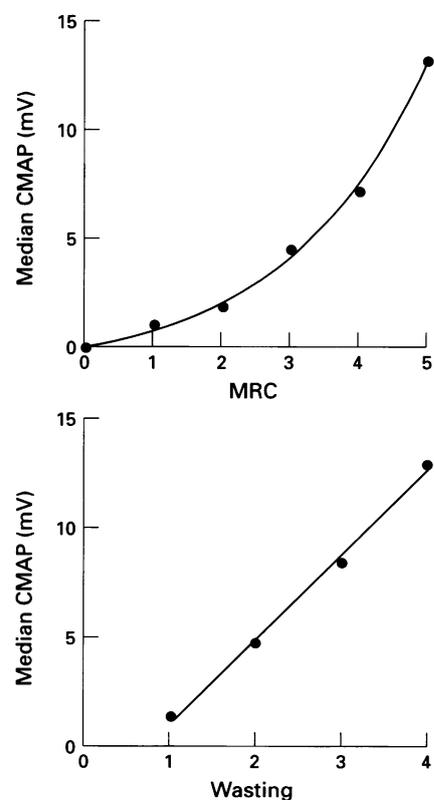
The force generating capacity of a muscle is directly related to the volume of active tissue.² The surface recorded CMAP represents the summation of all muscle fibre action potentials evoked in the muscle. Each fibre action potential at source will have an amplitude roughly related to the diameter of the fibre. The CMAP amplitude, therefore, will depend on the number of fibres generating action potentials and on the average single fibre action potential amplitude. The volume of excitable tissue in the muscle and the amplitude of the CMAP evoked by supramaximal nerve stimuli are therefore interrelated estimators of the force generating capacity of the muscle.

The CMAP amplitude is known to have a skewed distribution in healthy subjects; this was also true in the current series of mea-

surements. The median (rather than the mean) CMAP amplitude was therefore used as a measure of central tendency to relate to the MRC and wasting estimates. The figure shows a curvilinear relation between MRC score and CMAP amplitude. Given the arbitrary nature of definition of the MRC scale points, it is remarkable that the relation of MRC score to CMAP amplitude can be fitted so well by an exponential function ($y = -1.28(1 - e^{-0.48x})$, $r = 0.99$). In effect, a reduction of one point on the scale is associated, on average, with an approximate halving of CMAP amplitude. By contrast, the wasting score, equally arbitrary, is linearly related to CMAP amplitude ($y = 3.82x - 2.68$, $r = 0.99$).

Weakness of hand muscles in amyotrophic lateral sclerosis can be due to either a lower motor neuron lesion (LMN), an upper motor neuron lesion (UMN), or to a combination of the two. Weakness due to UMN lesion is not associated with wasting or a reduction in CMAP amplitude. It is pertinent to ask whether the curvilinear relation seen in the figure could be due to additional UMN weakness in some patients. At a given MRC scale point, if the weakness had a UMN component, CMAP amplitude would tend to be higher and the relation between MRC and CMAP would tend to be less curved, the reverse of what is actually found. The curvilinear relation between CMAP amplitude and MRC score is, therefore, not due to the effect of weakness resulting from UMN lesion.

Wasting could be due to a reduction in the number of active fibres or a reduction in diameter of fibres, or both. Clearly, wasting



The relation in the first dorsal interosseous muscle between MRC score and median CMAP amplitude (above) and wasting score and median CMAP amplitude (below) based on 183 observations from 40 patients with sporadic ALS. The curve relating MRC and CMAP has been fitted with an exponential function; the relation between wasting and CMAP is linear.

Life events in patients with Creutzfeldt-Jakob disease (CJD) and hospital controls

Type of life events	Patients with CJD (n = 55)	Controls (n = 55)
Death of close relatives: (husband or wife, siblings, parents, children, or grand children)	8	3
Major professional events: (unemployment, moving to another town)	7	0
Serious familial problem: (illness of a relative, serious familial conflict)	12	1