Depression as a major symptom of multiple sclerosis

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SUMMARY Thirty patients suffering from multiple sclerosis have been compared with 30 patients suffering from other chronic neurological diseases. The degree of disability was similar in these two groups. The patients with multiple sclerosis had experienced more episodes of severe depression both before and after the onset of neurological symptoms. The possible reasons for these episodes are discussed and it is concluded that in some patients serious affective disorder may be a presenting or complicating feature of multiple sclerosis.

"Suffering from depression . . . the melancholy fit fell very suddenly, all the colour went out of my life and the world was dirty grey." Thus wrote Barbellion (1919)¹; and, later, "Back to work—a terrible day—thoughts of suicide—a pistol. Returned to London very depressed. Am not so well as I was three weeks ago. The sight of my eye is affected . . . I have a numb feeling on one side of my face and my right arm is less mobile."

Barbellion's observations demonstrate that severe depression can both precede and accompany the neurological symptoms of multiple sclerosis. Nonetheless, it is generally assumed that any major disturbances of mood in patients with progressively incapacitating diseases like multiple sclerosis are understandable responses to stressful situations from which no permanent relief can be expected. Surridge² found no significant difference in the incidence of depressive symptoms in multiple sclerosis patients compared with controls suffering from muscular dystrophy, and concluded that the majority of the depressed multiple sclerosis patients were suffering from a psychogenic or reactive type of illness. On the other hand, there have been a number of reports of a high incidence of severe depression among multiple sclerosis patients. Braceland and Griffin,³ for example, claimed that 20% of their patients were depressed, and Pommé *et al*⁴ observed that some patients developed depression

which responded to drug therapy before the onset of neurological signs. One of O'Malley's patients,⁵ a 35 year old woman, had suffered two psychiatric breakdowns at the ages of 27 and 29 years, four years before developing multiple sclerosis. In the second illness, which lasted six months, she was depressed and suicidal. Young *et al*⁶ described prodromal psychiatric symptoms in five cases of multiple sclerosis, two of whom were depressed. Mür *et al*⁷ found that depression in multiple sclerosis patients often responded to appropriate treatment and that in some patients the psychiatric preceded the neurological symptoms. Goodstein and Ferrell,⁸ after surveying 200 papers on multiple sclerosis, found that only 15 reported the occurrence of affective disorder before the onset of neurological symptoms, but that none of the authors considered that depressive illness could be the presenting feature in multiple sclerosis. Their three patients had experienced recurrent bouts of depression for some years before neurological symptoms appeared. Clearly such illnesses could not be regarded as reactions to the disease. Kahana *et al*⁹ found that 18% of patients with cerebral multiple sclerosis were depressed and that 3% committed suicide, a rate that was 14 times greater than in the general Israel population. The significance of cerebral damage as a factor in the development of severe affective illness was brought out by the report of Bignami *et al*.¹⁰ This patient became depressed one month before neurological signs appeared. After a rapid progression of the disease he died, and at autopsy plaques were found in the hypothalamus, cerebral peduncles and pons. There was no past history of depression.

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In contrast with these findings, Cottrell and Wilson¹¹ found that 63% of their multiple sclerosis patients showed abnormal optimism; with the consequence that euphoria has ever since been regarded as one of the more typical features of the disease. Recent work^{2 12} has linked euphoria with intellectual deterioration which was detected in only 2% of Cottrell and Wilson's patients. There is, however, no evidence that precise psychometric studies were carried out to assess the degree of cognitive impairment.

When depressive illnesses antedate neurological symptoms it is very difficult to know whether the psychiatric illness was a chance event or an early manifestation of multiple sclerosis. In patients with many recurrences of depression over a period of years, particularly if there is a positive family history of affective disorder, one might reasonably argue that the subsequent development of multiple sclerosis is a coincidental finding unrelated to previous psychiatric illness. On the other hand, severe depression in a previously healthy patient, coming on shortly before the onset of neurological symptoms, suggests that the two conditions may be inter-related. Similarly one might assume that when depression occurs in a patient who, some years previously suffered a transitory neurological disorder with no permanent defect, but who later develops unequivocal signs of multiple sclerosis, the affective disorder could have been a manifestation of the disease. Once the illness is fully established and causing serious disabilities it is far from easy to decide whether any depressive symptoms are reactive or endogenous; in fact it seems unlikely that any single aetiological explanation is adequate. Furthermore, once the illness is established the effects of treatment may complicate the issue. Steroids are well known to cause depression in some patients and baclofen has also been reported to cause depression.^{13 14}

In an attempt to solve some of these problems we decided to investigate the psychiatric histories of multiple sclerosis patients and compare them with patients suffering from a variety of chronic neurological syndromes causing similar degrees of disability.

Methods

To ensure, as far as possible, fairly reliable recall of events before the onset of illness, we decided to include only patients with illnesses of not longer than five years' duration. A data collection sheet was used to record details of illness, the present mental

and physical state and depression experienced during the year before and subsequent to the onset of neurological symptoms. Unfortunately, the number of patients with multiple sclerosis who had been ill for five years or less was too small to provide an adequate sample and for that reason we included patients with illnesses of longer duration. However, we deliberately excluded patients who were showing signs of dementia in order to ensure that memory defects would not impair their recall of past events. Each patient was interviewed by the Research Psychologist (MMS) either in their own homes or at the Multiple Sclerosis Centre in Brisbane. An attempt was made to assess the patient's mood state at the time of interview and all patients completed the Beck Depressive Mood Inventory.¹⁵ We enquired about current medication, past illnesses, particularly psychiatric illnesses, and family history of psychiatric illness. Patients were encouraged to comment freely on any other matters not specifically included in the questionnaire.

The control patients were selected initially from patients attending the Multiple Sclerosis Centre suffering from other chronic or progressive neurological syndromes. Others were under the care of clinicians in private practice. They were matched for age and sex with the multiple sclerosis patients and included the following diagnoses: 10 patients with Friedreich's Ataxia and other hereditary cerebellar ataxias, three patients with muscular dystrophy, three with motor neurone disease, four with dystrophia myotonica, three with chronic polyneuritis and seven with miscellaneous diagnoses varying from myasthenia gravis to cerebral palsy. All the patients were examined in the same way as the multiple sclerosis patients and the data were recorded on the standard form.

Results

Table 1 shows the demographic characteristics of the two groups of patients. The patients and controls were well matched for age but more of the controls were single, largely because of the onset of their illness during childhood and adolescence in six cases. As already mentioned, we tried to select multiple sclerosis patients from those with illnesses of relatively short duration but this was not possible for the control patients, some of whom had been affected for significantly longer.

Disabilities Patients were assessed on a three point scale of increasing severity for disabilities affecting locomotion, manual skills, vision, speech and sphincter control. Other disabilities specifically mentioned by the patients were also recorded. The total disability score on each patient was obtained by adding together the scores on individual items. The maximum pos-

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Table 1 Demographic characteristics of the two groups

	Multiple sclerosis	Controls
Sex		
Male	12	12
Female	13	18
Age (yr)		
20-29	3	6
30-39	9	5
40-49	4	6
50-59	12	9
60+	2	4
Mean age	45.0	44.9
SD	11.55	12.91
Civil status		
Single	2	11
Married	21	14
Separated/divorced	4	4
Widowed	3	1
Chi-squared = 8.63; DF = 3, $p < 0.05$		
Duration of illness		
0-4 years	6	4
5-9 years	16	2
10-14 years	4	8
15 years and over	4	16
Chi-squared = 19.82; DF = 3, $p < 0.001$		

sible score was 21. The distribution of scores for patients and controls, shown in table 2, indicates that the multiple sclerosis patients and controls were well matched in terms of general disability.

The scores of patients and controls on the Beck Depressive Inventory were compared. These showed that at the time of interview the multiple sclerosis patients were significantly more depressed than the controls (table 3). We also compared the disability and depression scores with one another. For the multiple sclerosis patients the Kendall Rank Correlation Coefficient (τ) was 0.29 and for the controls, 0.28. Both findings are significant at the 5% level of probability, suggesting that the degree of depression could, to a limited extent, be related to the severity of the handicap.

Fourteen multiple sclerosis patients admitted to feeling sad and depressed when they were completing the Beck Inventory. Not surprisingly, their depressive scores were significantly higher than

Table 2 Disability scores

	0	1-4	5-9	10-14	15+
Multiple sclerosis patients	2	12	12	3	1
Controls	1	13	12	4	0

Table 3 Depressive inventory scores

	0-4	5-9	10-14	15-19	20-24	25+
Multiple sclerosis patients	5	8	9	4	1	3
Controls	14	10	5	1	0	0

Mann-Whitney Test: $Z = 3.87$, $p < 0.001$

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those who denied feelings of depression (Mann-Whitney Test, $Z = 3.74$, $p < 0.001$). Of the controls, two were moderately depressed, one severely so when interviewed. This patient, a 46 year old woman, suffered from a familial cerebellar degeneration complicated by epilepsy.

All patients and controls were asked a standard set of questions designed to elicit symptoms of depression. They were asked to state if they had experienced symptoms of this kind during the year before their neurological illnesses developed and whether they had occurred subsequently. Eight of the multiple sclerosis patients but none of the controls had suffered from depression before their neurological illnesses began. However, six of the control patients had developed their illnesses in childhood or during adolescence. It seems unlikely that severe depression would have affected any of these beforehand. Excluding these six and comparing the remainder with the multiple sclerosis patients, the difference is statistically significant (chi-squared = 7.51, $p < 0.01$). Two of the multiple sclerosis patients had experienced earlier transitory neurological symptoms which were not diagnosed at the time. Both these patients experienced severe depression during the year before the onset of their present chronic neurological illnesses. Sixteen of the multiple sclerosis patients and five of the controls had suffered from an endogenous type of depression since the onset of their illnesses (chi-squared = 8.86, $p < 0.005$).

We felt that the duration of illness might have contributed to the frequency and degree of depression in the multiple sclerosis patients, but no significant difference was found between patients who had been ill for five years or less compared with those who had been ill for longer periods of time. (Mann-Whitney Test, $Z = 1.24$, NS). We also considered whether the present level of disability was related to the past history of depression. Although the mean of the disability scores for the patients with past histories of depression was slightly higher than that of non-depressed multiple sclerosis patients, this difference was not statistically significant.

Could the differences between the multiple sclerosis and control patients be caused by potentially depressing drugs being taken by the multiple sclerosis patients or by the presence of concurrent diseases? Although more multiple sclerosis patients were taking drugs known to cause depression in some patients and, furthermore, had a greater number of other types of illness, neither variable differentiated significantly between these two groups of patients.

Discussion

We have shown that multiple sclerosis patients were significantly more depressed than a group of control patients, matched for age, sex and degree of disability, suffering from a variety of chronic neurological syndromes. In addition, more of the multiple sclerosis patients had experienced episodes of depression both before and since the onset of their illnesses. Whereas one might argue that some of those who developed depression did so as a reaction to the progress of the disease, one cannot use the argument to explain similar bouts of depression occurring shortly before neurological symptoms had developed or after a first manifestation of transitory symptoms that cleared completely without the diagnosis of multiple sclerosis being considered. If severe depression were an understandable reaction to a distressing disease, one has to ask why so few of the controls with equally distressing conditions remained relatively unaffected. Without doubt many of the multiple sclerosis patients found the sudden and unpredictable features of their illness disturbing and likely to arouse feelings of hopelessness and despondency. On the other hand, the control patients had either come to terms with their illnesses which had handicapped them for many years or, realising their slowly progressive nature in many cases, they could accept this more predictable course without undue distress. The effect of duration of illness on our multiple sclerosis patients' memories could have influenced our findings, but this did not appear to be the case as five patients with illnesses of less than six years' duration and four patients with illnesses of greater duration recalled depressive illnesses before the onset of neurological symptoms. Furthermore, six patients with illnesses of less than six years' duration and eight patients with longer experience of illness had suffered depression since the onset of multiple sclerosis. The quality and alleged causes of depression in the multiple sclerosis patients were also examined. It is well known that patients will attribute depression to environmental misfortunes whose true impact can only with difficulty be assessed retrospectively. For example, one patient who suffered from depression one year before the onset of neurological symptoms attributed her illness to the death of a parent four years earlier. One might consider her feelings of guilt and self-reproach over this loss as symptoms of a deep depression which included a sense of hopelessness and despair, broken sleep, anorexia, decline

in weight and energy and loss of libido. She continued to suffer bouts of depression over the six years following the onset of her neurological illness.

Nonetheless, some patients regarded their depressed mood and other psychological symptoms as understandable reactions to their illnesses and social difficulties. However, when responding to the questionnaire on depressive symptoms these patients gave evidence of an "endogenous" type of depression with characteristic vegetative symptoms, feelings of guilt, suicidal thoughts and diurnal mood change. Undoubtedly such a syndrome can follow major psychosocial stresses, but few of our patients could accurately pinpoint specific causes that could justifiably be regarded as essential precursors of psychiatric illness. On balance, we concluded that serious affective illness can be a premonitory symptom of multiple sclerosis or a complication that is likely to be secondary to cerebral damage caused by the disease. Possibly, in some patients, a true manic-depressive psychosis can be triggered off by multiple sclerosis. The patient described by Crémieux *et al*¹⁶ is a good example of manic-depressive disease associated with multiple sclerosis. At autopsy he was shown to have lesions in his temporal lobes, the thalamus and periventricular grey matter. We also know of a similar patient—not included in this series—a 40 year old man who first developed neurological symptoms at the age of 31 years. He subsequently suffered a number of acute attacks of mania and depression, in the last of which he committed suicide. He had made earlier suicidal attempts and was regarded as being seriously depressed when last seen before his death. At least one of our patients had attempted suicide and others had contemplated suicide. Manifestly the degree of depression will vary considerably along with other psychiatric symptoms present in some patients.

Personal accounts of serious depression in the course of multiple sclerosis probably tell us more about the true relationship between the affective disorder and the neurological syndrome. At least one doctor who had the misfortune to develop multiple sclerosis has courageously recorded how he became depressed but responded well to antidepressant medication¹⁷; and Barbellion's own account shows clearly how depression both preceded his illness and continued to plague him after it had developed.

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