Neurol Sci (2006) 27:S341–S343
DOI 10.1007/s10072-006-0656-1

U. Nocentini

Clinical assessment and therapy for depression

Abstract The occurrence of depression in multiple sclerosis (MS) patients is very high, with a lifetime prevalence of up to 50%. This co-occurrence has important negative consequences for MS patients. Until now, questions about the appropriateness of classification criteria and the reliability of assessment instruments have not been completely answered. At this time, it seems worthwhile to try to clarify these points considering their relevance for clinical and therapeutic approaches to treat MS and particularly to treat depression in MS. The risk of underestimating depressive symptoms is noted and appropriate treatment is strongly recommended. More recent antidepressant drugs are preferable in treating depression in MS patients because they have a better profile of side effects. At present, combined pharmacological and psychological therapy seems to be the best approach. Recently, rTMS was also proposed for treating depression in MS patients.

Key words Multiple sclerosis • Depression • Diagnosis • Assessment • Therapy

U. Nocentini (✉)
Cattedra di Neurologia
Università di Roma "Tor Vergata"
I.R.C.C.S. Fondazione "S. Lucia"
Via Ardeatina 306, I-00176 Rome, Italy
e-mail: u.nocentini@hsantalucia.it

Introduction

Two recent reports [1, 2] document the increased attention being dedicated to the study of depression in patients with multiple sclerosis (MS). Research activity not only concerns epidemiology but also the relationships among depression and various other aspects of MS (clinical course, disability and quality of life, neuroradiology, other mood disturbances, cognitive dysfunction, immunology and therapies). These papers report what is actually known about depression in MS and also raise many, still unanswered questions.

The questions and the possible answers

The questions can be summarised as follows: Is depression in MS patients a specific condition with the same aetiopathology or is it a reaction to an illness that affects all aspects of the person and of daily living?

The reason why it is so difficult to answer these questions becomes apparent if we look at standard diagnostic criteria for depression. At least four or five of the nine core symptoms in the diagnostic criteria for major depressive episode (MDE) in the DSM IV TR [3] (sleep problems, psychomotor retardation, fatigue, reduced concentration, reduced appetite with weight loss) can occur in MS independently of depression.

Paradoxically, all that is needed to surpass the five basic symptoms required for the diagnosis of depression is depressed mood or loss of interest in daily activities (and one of the two is obligatory).

Further, to examine the specificity/reactivity dilemma, let us consider two examples of differential diagnosis. The first example concerns MDE and the adjustment disorder (AD) with depressed mood. The limitation imposed on the diagnosis of MDE by its symptom commonality with MS makes it difficult to distinguish between the two diagnostic cate-

gories: conceptually, the experience of patients with AD is closely linked to that of patients with a disease like MS.

Second, let us consider MDE versus mood disorder due to a general medical condition: if the pathological processes underlying MS are also the cause of depression, this could be the appropriate diagnostic category.

Data for specifying depression in MS derive from a survey of the relevant literature [1, 2, 4]. A higher prevalence than in other chronic medical conditions, with estimates of lifetime prevalence rates of 40%–50%, has been reported; there are 7.5 times more deaths caused by suicide in this population than in the age-matched general population.

Similarities in the course of the illnesses, i.e., both can be relapsing or chronic, and the precipitating influence of stressful events are evocative.

Magnetic resonance imaging shows the prevalence of damage in depressed, compared to non-depressed, MS patients in the left anterior temporal/parietal regions as well as in the same regions of the right hemisphere. Therefore, no firm conclusions can be drawn.

The variation in cytokine profiles in both MS and depressed patients compared to normal individuals and the fact that successful treatment of depression is associated with suppression of some T-cell responses in MS are intriguing elements.

Moreover, the relationship between depression and cognitive dysfunction in MS deserves attention in the specificity *vs*. reactivity debate. Actually, depression is thought to negatively influence the more effortful processes of information processing and working memory; these processes are sustained by structures mainly located in the frontal lobes. Some areas of these lobes seem relevant for behavioural adjustment, i.e., in some MS patients direct damage to these areas or their disconnection from other areas can impair adjustment capacities and can therefore play a role in the development of depression.

Instead, those who believe that depression in MS is reactive base their argument on the relationship between depression and disability. Although not all studies have found this relationship, the absence of a correlation with the Expanded Disability Status Scale score can be explained as due to the fact that this score reflects spinal more than brain damage. Alternatively, greater disability should indicate greater cerebral involvement. Again, the higher prevalence of depression in patients with a relapsing–remitting (RR) and secondary progressive (SP) course compared to those with a primary progressive (PP) one may speak in favour of the role of cerebral damage in causing depression and may also be the consequence of the different psychological situation of the typical RR-SP MS patient compared to that of the typical PP MS patient [5].

Also, data on the lack of a genetic basis for depression in MS [6] may speak for both a specific and reactive mechanism, i.e., if a genetic predisposition is not present, something specific to MS (lesion location, immunological characteristics) may provoke depression. However, if this predisposition is lacking it may be a sign that there is nothing specific in the depression of MS patients and that it is a reaction to a serious illness.

But, how can we explain the higher prevalence of depression in MS compared to other serious and chronic illnesses in light of the reactive hypothesis? One reason for this prevalence may be the peculiarity of MS. No other disease impairs all functions, has an impact on all aspects of personal, family and social life and, at least in the majority of patients, can occur at an age when people are building their lives and rely on certainties that the disease suddenly destroys.

Despite the many difficulties and uncertainties involved, every effort should be made to solve the specificity/reactivity dilemma because of its influence on the approach to use for evaluation and therapy.

The problem of standardised assessment is also important for clinical practice. Assessment instruments are reliable if they can be used in screening activities and in the evaluation of treatment efficacy. Unfortunately, symptom commonality between MS and depression also creates problems for the development of assessment instruments; various solutions have been proposed (i.e., see [7]), but all need to be further investigated by means of clinical research.

However, the most important thing to learn from research and to adopt in clinical activity is that MS patients with depressive symptoms should be treated, because the consequences of mood disorders are very important for these patients [1, 2].

Pharmacological therapy

Before treating the topic of depression therapy in MS patients, it is important to examine the influence on mood of two categories of drugs very frequently administered to MS patients: corticosteroids and interferons (IFNs).

Corticosteroids can cause manic symptoms and precipitate a psychotic syndrome; a depressive mood switch after the end of a course of high-dose corticosteroids is also acknowledged. The occurrence of depressive symptoms has also been reported during the administration of corticosteroids [8].

The first large-scale trial with IFNβ-1b suggests a possible depressogenic effect of IFNs, with a higher suicide rate in the treated group than in the placebo group. Therefore, caution in using IFNs in MS depressed patients is strongly recommended. However, additional IFN trials have not confirmed this, showing that a previous history of depressed mood was the best predictor of depression in IFN-treated MS patients [2].

Controlled studies on the efficacy of antidepressant drugs in depressed MS patients are surprisingly scarce. One study

that is constantly cited is that on the tricyclic compound desipramine, a double-blind placebo-controlled study that established the superiority of the drug over the placebo [9]. Another study [10] compared the selective serotonin reuptake inhibitor (SSRI) sertraline with two psychotherapeutic approaches, individual cognitive-behavioural therapy (CBT) and supportive-expressive group therapy, showing a significantly superior effect of both the drug and the CBT over the other psychotherapeutic approach.

Other open-label trials have shown the efficacy of sertraline or of the reversible monoamine oxidase inhibitor (RIMA) moclobemide [1, 2].

Although experimental studies are few, it is generally agreed that antidepressant drugs are effective in the treatment of depressed MS patients; preference is given to more recent drugs like SSRI because of their better side-effects profile. However, more well-designed studies are needed because the efficacy levels reported in some studies [10] are far from satisfactory and even the SSRI can have side effects that are particularly deleterious for MS patients [2].

A great deal of knowledge has been collected in past years in the field of psychopharmacology of depression, and this knowledge seems applicable in the treatment of MS patients. In particular, it has emerged that serotonin and noradrenalin can have different weights in the psychic and somatic aspects of depression. Clinical data seem to support this point, because drugs acting on more neurotransmitters (RIMA) but not SSRIs are effective in the treatment of pathologies (like chronic fatigue syndrome) in which somatic complaints are very high.

Although psychotherapy will be treated elsewhere in this volume, we must say that there is a consensus in the literature on the importance of an integrated approach involving psychotherapy and antidepressant drugs.

Finally, there may be another possibility for depressed MS patients, in particular in cases in which pharmacotherapy, psychotherapy and a combination of the two does not reach a satisfactory level of efficacy or the use of drugs is contraindicated. This possibility is offered by repetitive transcranial magnetic stimulation (rTMS); it is suggested by its actual use in "idiopathic" depression and its possible use in depressed neurological patients (for a very recent review of this topic, see [11]).

References

1. Goldman Consensus Group (2005) The Goldman Consensus statement on depression in multiple sclerosis. Mult Scler 11:328–337.
2. Siegert RJ, Abernethy DA (2005) Depression in multiple sclerosis: a review. J Neurol Neurosurg Psychiatry 76:469–475
3. American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders – DSM IV TR. American Psychiatric Publishing, Inc., Arlington, VA
4. Joffe RT (2005) Depression and multiple sclerosis: a potential way to understand the biology of major depressive illness. J Psychiatry Neurosci 30:9–10
5. Zabad RK, Patten SB, Metz LM (2005) The association of depression with disease course in multiple sclerosis. Neurology 64:359–360
6. Sadovnick AD, Remick RA, Allen J et al (1996) Depression and multiple sclerosis. Neurology 46:628–632
7. Solari A, Motta A, Mendozzi L et al (2003) Italian version of the Chicago multiscale depression inventory: translation, adaptation and testing in people with multiple sclerosis. Neurol Sci 24:375–383
8. Brown ES, Chandler PA (2001) Mood and cognitive changes during systemic corticosteroid therapy. Primary Care Companion J Clin Psychiatry 3:17–21
9. Schiffer RB, Wineman NM (1990) Antidepressant pharmacotherapy of depression associated with multiple sclerosis. Am J Psychiatry 147:1493–1497
10. Mohr DC, Boudewyn AC, Goodkin DE et al (2001) Comparative outcomes for individual cognitive-behavior therapy, supportive-expressive group psychotherapy and Sertraline for the treatment of depression in multiple sclerosis. J Consult Clin Psychol 69:942–949
11. Fregni F, Pascual-Leone A (2005) Transcranic magnetic stimulation for the treatment of depression in neurologic disorders. Curr Psychiatry Rep 7:381–390