CHAPTER 3

Depression

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INTRODUCTION

Of the mental changes associated with multiple sclerosis (MS), depression, in its various forms, is by far the most prevalent. Depression is also one of the most important factors that negatively affect the subject quality of life, beyond the level of physical impairment and disability (Amato et al., 2001). Significant depression has been described in early-onset patients newly diagnosed with MS (Solari et al., 2001). It is therefore important that clinicians have a good understanding of how the syndrome may present, what the underlying factors are and what’s the best way to approach treatment.

In this chapter we will discuss the definition, prevalence and clinical characteristics of this disorder as well as the physiopathology of MS-related depression and the main treatment options.

DIAGNOSIS AND PREVALENCE

The clinical criteria for the diagnosis of major depression in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) are presented in Table 3.1. In order to pose a diagnosis of major depression it is necessary that five or more of the above symptoms are present during a minimum period of two weeks.

The diagnosis of depression can be posed on the basis of the traditional clinical interview, including interviews that are structured to detect major depression. Moreover, there are other self-report rating scales that can be used. It is important to note that self-report scales are designed to screen depressive symptoms rather than to make a clinical diagnosis. Moreover, when these scales are used in patients with chronic disease conditions like MS, it is likely that a few somatic symptoms listed in the depression scales overlap with symptoms of MS itself. Examples are symptoms such as fatigue, sleep disturbance and impairment in concentration and cognitive faculties, that can be observed in both conditions. To deal with this issue, rating scales have been developed specifically to be used in a medical setting.
Criteria for the diagnosis of major depression (American Psychiatric Association, 1994).

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<th>Five or more of the following symptoms during the same two week period:</th>
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<td>1. Depressed mood most of the day</td>
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<td>2. Markedly diminished interest or pleasure in all activities</td>
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<td>3. Significant weight loss, or weight gain (5% of body weight in a month)</td>
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<td>4. Insomnia or hypersomnia nearly every day</td>
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<td>5. Psychomotor agitation or retardation (observable by others)</td>
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<td>6. Fatigue or loss of energy nearly every day</td>
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<td>7. Feelings of worthlessness, excessive, inappropriate guilt</td>
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<td>8. Diminished ability to think or concentrate</td>
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<td>9. Recurrent thoughts of death</td>
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Among these, the most widely used are the Beck Fast Screen for medically ill patients and the Hospital Anxiety and Depression Scale that have been validated to be used in MS patients. In clinic-based samples the lifetime prevalence of major depression is up to 50% in patients with MS (Minden and Schiffer, 1990). These data are confirmed in a community-based study performed in Canada, where the 12-month prevalence rate of major depression was significantly higher than that observed in the general population (the adjusted odds ratio was 2.3) (Patten et al., 2003) as well as in other more recent prevalence surveys (Jones et al., 2012; Wood et al., 2012).

So-called “subsyndromal depression”, represented by clusters of depressive symptoms that do not fulfill the diagnostic criteria for major depression, is also common in the MS population and is associated with significant psychological distress.

The importance of detecting and treating depressed patients is underscored by the high suicide rate in MS. In particular, in a Canadian study, the proportion of suicides among MS deaths was 7.5 times higher than in the age-matched general population (Sadovnik et al., 1991).

Several rating scales for depression are used both in clinical practice and research purposes. Among scales administered by the psychiatrist, the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960) and the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) are largely used in the MS literature. Among self-administered scales, the Beck Depression Inventory (BDI) is widely used and well validated. One problem with the use of these scales in MS is the possible overlapping between depression symptoms and neurological symptoms. The Beck Depression Inventory-Fast Screen (BDI-FS) is an abbreviated, seven-item version of the BDI that excludes somatic symptoms and has been validated in MS for screening purposes (Benedict et al., 2003). Another self-administered scale specifically validated in the MS population is the Chicago Multiscale Depression Inventory (CMDI) (Nyenhuis et al., 1998), also translated and validated in an Italian MS population.

Pathophysiology

The pathophysiology of MS-related depression is most probably multifactorial. There is no evidence to date to confirm a definite genetic link between MS and unipolar
depression. However, evidence is controversial with respect to depression occurring as a part of bipolar affective illness (Joffe et al., 1987). Depression in MS patients is often associated with cognitive impairments and fatigue, possibly due to a common physiopathological basis (Amato et al., 2001).

Over the past two decades the biological basis of depression in MS has been addressed in magnetic resonance imaging (MRI) studies. MRI studies have documented an association between depression and various MRI features, including total T2 lesion volume (Berg et al., 2000), regional T2 lesions (Pujol et al., 1997) and T1 lesions (Bakshi et al., 2000), as well as regional brain atrophy (Bakshi et al., 2000).

The combination of these MRI variables was found to account for nearly 40% of the depression variance (Feinstein et al., 2004). Significantly, the lesions and atrophy were mainly localized in the anterior temporal and medial frontal regions.

Moreover, a dysfunction of the hypothalamic-pituitary-adrenal axis has been involved in the pathogenesis of depression. In this regard, Gold et al. (2010) have recently reported that depressed MS patients had abnormally elevated cortisol levels and smaller volumes of the dentate gyrus, in particular in the cornu ammonis region. In another study, Feinstein et al. (2010) used diffusion tensor imaging (DTI) to show that MS patients with depression were more likely to have pathological changes in normal appearing white and grey matter, again localized in the anterior temporal regions.

Finally, in a recent fMRI study (Passamonti et al., 2009), MS patients compared with healthy controls showed evidence of changes in activity and functional connectivity in areas that are critical in regulating mood and affecting areas such as the amygdala and the ventrolateral and medial prefrontal cortex.

The psychosocial components of MS-related depression are also relevant and extensively addressed in the literature. Many psychosocial aspects can play an important role, including uncertainty related to a disabling condition that has a largely unpredictable course, restriction of social contacts and activities, feelings of helplessness, dysfunctional coping strategies developed to deal with disease-related challenges and fatigue. When various psychosocial factors are combined, they account for approximately 40% of the depression variance (Lynch et al., 2001), a figure comparable to that reported in MRI research.

**TREATMENT**

Depression can respond to pharmacological approaches, cognitive behavioral treatment and psychotherapy.

A double-blind, placebo-controlled study revealed the efficacy of the tricyclic drug desipramine in treating depression in MS subjects. A drawback was the presence of anticholinergic side effects in few patients, which limited their ability to take therapeutic doses of the drug (Schiffer and Wineman, 1990).

This result was replicated in a series of open-label trials with serotoninergic reuptake inhibitor (SSRI) drugs, where tolerability was better than that reported in the tricyclic trial. The SSRI are also safer when taken in overdose. One limitation of SSRI is however represented by sexual dysfunction. Furthermore, a recent double-blind, placebo-controlled study with paroxetine reported benefits that were not statistically significant (Ehde et al., 2008).
In patients who do not respond to antidepressants, lithium, antiepileptic drugs (e.g. carbamazepine, gabapentin, valproate) and augmentation of antidepressant medication may prove effective (Falk et al., 1979). A recent systematic review covers the most relevant studies in the field (Koch et al., 2011).

For patients who cannot tolerate medication or who are reluctant to take it, cognitive behavioral treatment (CBT) offers a useful alternative option (Mohr et al., 2001). While the treatment benefits are still apparent up to six months following treatment cessation (Mohr et al., 2001), no longer-term data are available.

Another approach is represented by psychotherapy that may prove a useful addition to antidepressant medication in more severe cases. Psychotherapy can be pursued either individually or within a group. The psychotherapy approach can range from simple support to more insight-oriented therapy, depending on the patient’s needs and cognitive abilities (Minden, 1992). The flexibility also extends to the duration of treatment, which may consist of a single session or a long-term therapy, depending on the patient’s characteristics (Minden, 1992). Beyond anecdotal evidence, an experimental study (Crawford and McIvor, 1985) showed a significant mood improvement in a group of patients undergoing insight-oriented psychotherapy compared with a group undergoing unspecific treatment and a group not being treated.

Finally, in selected patients with severe depression, refractory to multiple treatments and who are at high risk of suicide, electroconvulsive treatment is used in a few psychiatric centres. In MS subjects this treatment might precipitate a clinical relapse. It has been suggested that in these patients the presence, before treatment, of gadolinium enhancing lesions at MRI represents a risk factor for disease reactivation (Mattingley et al., 1992).

CONCLUSIONS

It needs to be emphasized that depression is highly prevalent in MS people and represents a considerable source of morbidity and mortality and one of the main determinants of quality of life. Missing the diagnosis is damaging for the patient, more so as the disorder can, in the majority of the patients, be successfully treated.

REFERENCES


