Depression and multiple sclerosis:
a potential way to understand the biology
of major depressive illness

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It has long been known that a variety of medical disorders may present with depressive symptoms or syndromes and that depression may influence the course of medical disorders. For example, depression is a risk factor for ischemic heart disease and may also influence prognosis after acute myocardial infarction. Moreover, various endocrine disorders, particularly thyroid disease and especially hypothyroidism and diseases of the hypothalamic–pituitary–adrenal axis, may be associated with a wide range of psychiatric symptoms and, more particularly, depression. These observations have provided an opportunity to use medical illnesses to understand the pathophysiology of primary depressive illness. The association of multiple sclerosis and depressive symptoms and disorders may provide yet another opportunity and should not be overlooked.

Multiple sclerosis is a chronic, inflammatory demyelinating disorder of the central nervous system. The disorder is one of the most common neurologic disorders to affect young adults and, although its cause is not fully understood, it appears to involve a complex interplay of genetic, environmental and immunologic factors. Several studies have documented an increased prevalence of lifetime diagnoses of major depressive disorder in patients with multiple sclerosis. Recently, a large-scale community epidemiologic study reported that about 40% of subjects had clinical depressive symptoms. This is consistent with numerous earlier studies conducted largely in specialty clinics that have reported a lifetime risk of major depression of 25%–50% in patients with multiple sclerosis. Moreover, Feinstein reported a substantially higher risk of suicidal behaviour in patients with multiple sclerosis that is consistent with the high risk for major depression. Whether the occurrence or the severity of depressive symptoms are related to the severity of multiple sclerosis or the degree of disability still remains a controversial issue; however, the high co-occurrence of multiple sclerosis and depression is impressive.

There are several analogous features to these 2 disorders that are intriguing. The first, beside the obvious fact that both are disorders of the central nervous system, is that both have multifactorial causes, which involve the interplay of complex genetic and environmental factors. Second, both illnesses have a chronic and/or relapsing course. Third, stressful life events are moderately associated with both exacerbations of multiple sclerosis and episodes of recurrence in major depressive disorder. Last, immune phenomena may be involved in the biologic underpinnings of both these disorders. In both animal models and humans, certain T-cell responses activated by specific myelin antigens have been implicated in the cause of multiple sclerosis. The proinflammatory cytokine, interferon-γ, which is produced by T cells, is a major effector mechanism in the autoimmune process leading to the pathogenesis of the disorder. Depression has been associated with both increases in interferon-γ as well as in the subclasses of T cells involved in multiple sclerosis. Therefore, autoimmune phenomena may be one of the underlying factors linking depression to multiple sclerosis. The immune phenomena associated with depression may, in fact, exacerbate multiple sclerosis or they may be causative mechanisms common to both illnesses. Consistent with the former notion is the fact that successful treatment of depression is associated with suppression of both nonspecific and antigen-specific T-cell responses in multiple sclerosis.

The depression associated with multiple sclerosis is amenable to treatment both with psychotherapy as well as with antidepressants. At the very least, vigorous treatment of the depression may not only relieve current suffering and dysfunction but may also improve long-term prognosis for the depression and even the multiple sclerosis. This suggests that early psychiatric consultation and intervention should be the appropriate standard of care for patients with multiple sclerosis.
sclerosis who have depressive symptoms or depressive disorders. However, the tantalizing suggestion of common biologic mechanisms indicates that the co-occurrence of these disorders may be fruitful in shedding light on our understanding of the pathogenesis of primary major depressive disorder.

Early observations, more than 100 years ago, of the link between adrenal and thyroid endocrinopathies and psychiatric illness has allowed major advances in our understanding of the biology of depressive disorders. Our discovering of hypothalamic–pituitary–adrenal axis dysregulation in depression has been important in understanding the biology of the disorder and may also yield potential new therapeutic interventions in the form of the corticotropin-releasing hormone antagonists. Further close study of patients with multiple sclerosis and their high depressive morbidity may be of substantial advantage not only to those patients who suffer an enormous burden of illness but also to depressed patients in psychiatric clinics, both in terms of understanding their illness and in developing new therapeutic options.

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References