

# Axons, Cells, and Depression: The Nexus of Neurology and Psychiatry in Multiple Sclerosis

By Jack M. Gorman, MD, and Jennifer Finkel, MD

In many ways, multiple sclerosis (MS) is among the most frustrating and vicious of human diseases. Although we can readily see the demyelinating effect of MS lesions on postmortem examination, the diagnosis during life is fraught with difficulty. Advances in cerebrospinal fluid analysis and neuroimaging techniques have contributed to a recent revision of diagnostic criteria for MS, yet the majority of patients still wait for years until a definitive diagnosis is reached. They then face a disease that is both highly unpredictable and, in most cases, severely debilitating.

The unpredictable nature of MS is particularly distressing and many patients exist in a persistent state of fear and anxiety about their next MS exacerbation. Despite improved treatments, MS leaves some of the most severely affected patients wheelchair-bound by their early twenties. The more fortunate ones learn to deal with sporadic functional impairments for the rest of their lives. The unpredictable nature of MS leaves its victims always wondering about the next phase of their illness. For some, a more negative but definitive prognosis would be easier to accept than one for which the outcome is so unclear.

To make matters worse, the cause of MS remains an elusive one. Research points to an infectious and/or autoimmune etiology. The disorder is more common among those living in northern hemispheres, afflicts women more often than men, and has a partial genetic basis as evidenced by a greater concordance rate for monozygotic than dizygotic twins that nevertheless, falls far short of what would be expected of an autosomal, Mendelian disease. Drugs that modulate the immune system, from steroids to interferons, are somewhat helpful. Yet despite this, the long-term prognosis for MS has not changed much in recent decades and no therapy exists that addresses the root pathophysiology of the disease—demyelination.

For many years, neuroscientists ignored any type of cell in the central nervous system (CNS) that was not a neuron. We all learned in our basic neuroanatomy course in medical school that oligodendrocytes myelinate axons in the CNS and Schwann cells do so in the

peripheral nervous system. Yet the biology of oligodendrocytes has largely been ignored. Recently, however, this has changed. Genes involved in the regulation of myelin have been identified and strategies that may induce these genes to become more active are under study. Someday, it may be possible to figure out how to induce oligodendrocytes to re-myelinate axons in MS patients.

Until then, it seems that patients with MS have legitimate reasons to feel depressed. Indeed, depression is the most common psychiatric illness in patients with MS, occurring at much higher rates than found in the general population or in patients with chronic medical and neurological illnesses. The stress of living with an unpredictable and impairing disorder is more than enough stress to cause recurrent major depression.

However, a “reactive depression” may be a simplistic explanation for the high rates of depression in MS patients. The characteristic destructive lesions of MS occur in multiple brain regions thought to be associated with depression. Therefore, the possibility exists that depression in patients with MS occurs at least in part, secondary to MS plaques disrupting the neural pathways that are important in regulating mood. Signal hyperintensities in deep white matter have been linked to so-called “vascular depression” in geriatric patients, which suggests that some interference with white matter that affects normal axonal-neuronal conduction might be a cause of depression. At present, these thoughts are unproven speculations, but researchers have embarked on neuroimaging studies aimed at trying to understand whether the high correlation between MS and depression exists because of the stress of a chronic illness, disruption of axonal function, or both.

The articles in this month's *CNS Spectrums* go a long way toward helping us understand the complex emotional and cognitive abnormalities that are seen in MS. These should remind neurologists and psychiatrists alike that despite the fact that there may be an understandable “reason” for a patient to be depressed, depression in the context of chronic debilitating illness is nevertheless a highly complex experience that war-

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*Dr. Gorman is the editor of this journal and Esther and Joseph Klingenstein Professor of Psychiatry and chair of the Department of Psychiatry at Mount Sinai School of Medicine in New York City. Dr. Finkel is an associate in the Department of Psychiatry at Mount Sinai School of Medicine.*

rants clinical attention. Treatment with psychopharmacologic tools can be useful for depression in MS and antidepressant therapies will help many patients cope.

However, antidepressant therapy may not be the only answer. It is also essential to acknowledge the importance of psychosocial interventions in MS, not only for those directly affected but also for the family members of the diagnosed patient. Patients and their families need to be educated about what to expect

from the disease and to be prepared for the complicated emotions they may experience. Furthermore, patients need to be able to feel comfortable discussing their limitations and fears with clinicians as well as with loved ones. In our experience, a comprehensive psychosocial approach to the MS patient, including frequent psychotherapy as well as the involvement of a strong support network can sometimes obviate the need for medication. **CNS**

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From left to right: Jack M. Gorman, MD, editor of *CNS Spectrums* and member of the ADAA Board of Directors, Philip C. Kendall, PhD, ABPP, of Temple University, Darren L. Brodeur, CEO and publisher of MBL Communications, Inc., and Barbara O. Rothbaum, PhD, of the Emory University School of Medicine

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