The dramatic advances in neuroscience that have occurred in the last two decades, as exemplified by the burgeoning literature in functional and structural brain imaging and molecular neurobiology, have been paralleled by just as remarkable advances in immunology. It is not, therefore, surprising that connections between these two highly evolved complex communication systems would be sought, recognized, and explored to elucidate the pathophysiology of major psychiatric and neurological disorders. There is increasing evidence for imbalance of the immune system in the pathogenesis of a variety of neurological disorders including multiple sclerosis, anti-NMDA (N-methyl D-aspartate) receptor encephalitis, and myasthenia gravis. Indeed, an extensive bidirectional communication between the immune and nervous systems has now been unequivocally demonstrated.

The fundamental goal of this issue is to focus on recent advances in research that seek to determine whether links exist between major psychiatric disorders and immune system dysfunction, more specifically inflammation and mood disorders. Although there is increasing evidence for a role for inflammation in the pathophysiology of schizophrenia and bipolar disorder, the vast majority of work in this field has focused on major depression.

This issue of *Psychiatric Annals* is comprised of two basic science reviews of inflammation, one a primer on inflammation for psychiatrists by Dr. Éléonore Beurel, and the other a review of the seminal role of microglia, the primary immune cells in the central nervous system by Dr. Tina C. Franklin and colleagues. They describe the critical role of microglia in neuronal development and in normal synaptic function in the adult brain, as well as mechanisms underlying abnormal activation of microglia that can lead to excessive inflammation that contributes to depressive behaviors. Readers armed with this knowledge will likely better appreciate the three articles that follow. Emily Boorman and colleagues describe the complex findings of increased inflammation in mood (and to a lesser extent, anxiety) disorders with a focus on the overlap of depressive symptoms with so-called “sickness behavior” associated with the inflammatory response. They describe the evolving work on anti-inflammatory agents as novel antidepressants. Dr. M. Beatriz Currier comprehensively reviews the evidence for inflammation as the primary pathophysiological mechanism responsible both for the increase in depression in patients with many major medical disorders (cancer and cardiovascular disease and we would add diabetes and stroke to this growing list), and also for the poor outcomes associated with comorbid depression and these diseases. Finally, a provocative review by two leaders in the field, Drs. Charles L. Raison and Andrew H. Miller, concludes that anti-inflammatory agents may not have broad application as antidepressants compared to, for example, the selective serotonin reuptake inhibitors but rather possess efficacy only for depressed patients who exhibit laboratory evidence of inflammation. One of the most important points they make is that anti-inflammatory agents are not uniform in their mechanism of action and lumping nonsteroidal anti-inflammatory drugs together with cytokine antagonists,
for example, is problematic. Most importantly, they remind us of the importance of inflammation and the likelihood that there is a “sweet spot” or optimal level of inflammatory activity as regards to mood state, likely due to the requirement for microglia and cytokines in normal brain function.

The entire subject falls within the emerging field of personalized medicine—the idea that a subset of depressed patients, those with clear evidence of depression, are optimally treated, at least in part, with anti-inflammatory agents, represents a novel and exciting direction in psychiatry.

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