



## Full Length Review

## Immune suppression and immune activation in depression

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## ABSTRACT

Depression has been characterized as a disorder of both immune suppression and immune activation. Markers of impaired cellular immunity (decreased natural killer cell cytotoxicity) and inflammation (elevated IL-6, TNF $\alpha$ , and CRP) have been associated with depression. These immunological markers have been associated with other medical illnesses, suggesting that immune dysregulation may be a central feature common to both depression and to its frequent medical comorbidities. Yet the significant associations of findings of both immune suppression and immune activation with depression raise questions concerning the relationship between these two classes of immunological observations. Depressed populations are heterogeneous groups, and there may be differences in the immune profiles of populations that are more narrowly defined in terms of symptom profile and/or demographic features.

There have been few reports concurrently investigating markers of immune suppression and immune activation in the same depressed individuals. An emerging pre-clinical literature suggests that chronic inflammation may directly contribute to the pathophysiology of immune suppression in the context of illnesses such as cancer and rheumatoid arthritis. This literature provides us with specific immunoregulatory mechanisms mediating these relationships that could also explain differences in immune disturbances between subsets of depressed individuals. We propose a research agenda emphasizing the assessment of these immunoregulatory mechanisms in large samples of depressed subjects as a means to define the relationships among immune findings (suppression and/or activation) within the same depressed individuals and to characterize subsets of depressed subjects based on shared immune profiles. Such a program of research, building on and integrating our knowledge of the psychoneuroimmunology of depression, could lead to innovation in the assessment and treatment of depression and its medical comorbidities.

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## 1. Introduction

According to projections by the World Health Organization (WHO), by the year 2030 depression will result in more years of life lost to disability than any other illness (World Health Organization, 2008). Compounding the enormous burden of depression alone, there is an increasing recognition of a high prevalence of comorbidity between depression and many of the major medical illnesses of our time (e.g., heart disease, stroke, cancer, and HIV/AIDS), evidence that depression is a risk factor and negative prognostic indicator for many of these illnesses, and an emerging consensus that the relationship between depression and these illnesses is bidirectional

and, at least in part, driven by several biological processes, including immune dysregulation (Anisman et al., 2008; Evans et al., 2005). At the same time, the onset of the HIV epidemic and the recognition of the role of inflammation in the pathogenesis of heart disease (Hansson, 2005), stroke (Grau, 1997; Vaughan, 2003), and Alzheimer's disease (Aisen and Davis, 1994; Wyss-Coray, 2006) have established a central role for the immune system across the gamut of chronic diseases.

These three important trends—the growing impact of major depression, its increasingly recognized co-occurrence with many other medical illnesses, and the elucidation of immune processes in the pathogenesis of these same illnesses—highlight the potential clinical relevance of the study of the relationship between depression and the immune system. As it has developed over the past 30 years, the field of the psychoneuroimmunology of depression has been dominated by two sets of observations. The first set of observations concerns itself with the association between stress

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