

## Introduction

# Understanding Depression and Its Treatment: Restoration of Chemical Balance or Creation of Conditions Promoting Recovery?

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Whether antidepressants exert their action by correction of a monoamine deficiency or lesion or by upregulation or augmentation of intact monoamine systems is a matter of some debate. A satellite symposium entitled “Understanding Depression: Restoration of Chemical Imbalance or Augmentation of Social Functioning?” was held on October 31, 1998, at the 11th Congress of the European College of Neuropsychopharmacology (ECNP) in Paris, France, to explore the evidence for both sides of this argument. Following an overview of the history and evolution of the monoamine hypothesis of depression, the case for each viewpoint was presented, supported by talks covering the clinical and biochemical evidence.

The monoamine hypothesis of depression predicts that the underlying pathophysiologic basis of depression is a deficiency of central noradrenergic and/or serotonergic systems. Although antidepressant agents that elevate the levels of these neurotransmitters in the brain have all been shown to alleviate depressive symptoms, whether or not there is clear, convincing evidence for a primary lesion of a specific monoamine system in patients with depression is controversial. In fact, there is experimental evidence that antidepressants in current use may actually require intact monoamine systems for their therapeutic effect, and an alternative theory has been put forward that hypothesizes that antidepressant efficacy may stem from an ability to elicit conditions that promote recovery from symptoms.

The development of novel antidepressants has helped to provide a greater understanding of the neurochemistry of depression. It is becoming clear that the clinical efficacy of those medications, rather than being broadly equivalent, in fact varies. Although selective serotonin reuptake inhibitors (SSRIs) have been welcomed, largely due to their superior tolerability profile compared with the older antidepressants, agents that include a noradrenergic mode of action may offer superior efficacy in patients with severe depression and with respect to social functioning. With the advent of reboxetine, the first selective norepinephrine reuptake inhibitor (selective NRI), it will be possible to investigate the clinical relevance of modulation of the noradrenergic system.

The articles presented in this supplement summarize our current understanding of the mechanisms underlying depression, which will have benefit in terms of our approach to antidepressant therapy.

This supplement is the first of its kind as its contents meet both U.S. and European CME guidelines for educational materials.

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