INTRODUCTION

# Defeating the Dementors

DEPRESSION IS A DEVASTATING DISEASE. IT AFFECTS NOT ONLY THE DIRECTLY afflicted but also the people around them, their families, and their closest relations. It indiscriminately hits all strata of society, no matter one's intellectual background, age group, or economic situation. There are many cases of highly successful and widely admired individuals who have been struggling with depression for years. Unfortunately, for reasons we still do not fully understand, this condition has been on the rise over the past decades. Considering its impact on an individual's quality of life and subsequently on the economy and society in general, gaining an understanding of what causes depression and trying to develop effective therapies is of utmost importance. Hence, this year's Neuroscience Special Issue is devoted to different aspects of depression.

Duman and Aghajanian (p. 68) review evidence from basic and clinical studies that stress and depression cause neuronal atrophy and decreased synaptic connections in cortical and limbic brain regions. Antidepressants can block or reverse these neuronal deficits, although typical antidepressants have limited efficacy; however, novel rapidly acting antidepressants produce a fast induction of synaptogenesis and quickly reverse synaptic deficits caused by chronic stress. Together, these findings support a synaptogenic hypothesis of depression and treatment response.

Newly generated neurons are required for mood control and for the beneficial effects of antidepressants. Understanding adult neurogenesis may therefore provide a road map for the development of new treatments for depression. Introducing the concept of the neurogenic interactome, Eisch and Petrik (p. 72) synthesize recent seminal findings relevant to neurogenesis, with special emphasis on the interchange between stress, depression, and cognition.

Developing a suitable animal model is often an important step for understanding the basic mechanisms underlying a disease. Berton *et al*. (p. 75) summarize the current models for mood disorders and attempt a prospective analysis of potential tests or tools that might be implemented to improve our repertoire of such models for depression. The problem of animal models is also touched on in an article on why mental illnesses are so hard to treat, part of a Mysteries of the Brain package in the News Focus section, starting on p. 30.

However, not all is bleak. There are individuals who overcome difficult situations and show astonishing resilience in the face of adverse circumstances and other forms of acute or chronic traumatic stress. Studying them might provide us with clues about what can go right. Southwick and Charney (p. 79) provide an overview of current ideas about why some people are more protected against stress and depression than others and how this knowledge may help us develop better treatments and successful prevention strategies.

In *Science Signaling*, Shah describes evidence that hyperpolarization-activated, cyclic nucleotide–gated channels may be therapeutic targets for the treatment of depression, and Anisman and Hayley describe how targeting inflammatory mediators may enhance the efficacy of conventional therapies for depression.
— PETER STERN

## Depression

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*See also Editorial p. 15; News Focus section p. 30; Review p. 60; and Science Signaling, Science Careers, and Science Podcast at www.sciencemag.org/special/depression*

*Science*

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Peter Stern

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