

Neuroplasticity: A New Window on Therapeutics in Neuropsychiatric Disease

Over the last 20 years an understanding has emerged that the brain is in a state of continual change and adaptation to the environment. Notably, the cellular processes mediating brain adaptation are now seen as potential vulnerabilities underlying neuropsychiatric disorders. Neuroplasticity is the term widely used to describe this changing brain function at all levels of organization, from genetic to cellular and to behavioral.

This volume endeavors to inform neuroscientists and clinicians about the basic mechanisms of neuroplasticity that have been uncovered over the last half decade, and to describe how these mechanisms apply to common neuropsychiatric disorders. Thus, the first two contributions introduce the reader to some of the recently emerging cellular mechanisms of neuroplasticity, first at the level of epigenetic regulation of gene expression (McClung and Nestler), and second at the level of synaptic plasticity (Citri and Malenka). The next three chapters explore the integration of molecular plasticity into the neural circuits regulating behaviors that are critical for normal adaptive response to the environment; these include interactions between BDNF and serotonergic systems (Martinowich and Lu), prefrontal cortical circuitry (Moghaddam and Homayoun) and the circuitry underlying learning and retrieval of information (Quirk and Mueller). Building upon this foundation, the subsequent contributions specifically apply the biology of neuroplasticity to various neuropsychiatric disorders, including fragile X (Bear *et al*), depression (Pittenger and Duman), bipolar disorder (Schloesser *et al*), anxiety (Leonardo and Hen), schizophrenia (Lewis and Gonzalez-Burgos), addiction (Kalivas and O'Brien), and pediatric disorders (Rapoport and Gogtay).

By focusing on specific diseases, the authors not only show the reader how our evolving knowledge of neuroplasticity is revolutionizing our understanding of disease etiology, but also how this knowledge is creating the possibility of novel pharmacological and behavioral therapies. Toward this end, the neuropsychiatric disorders are treated first as diseases with molecular underpinnings that are susceptible to environmental and genetic regulation. These molecular underpinnings expose targets for the development of novel pharmacotherapeutics. The next level of integration is through brain circuitry, particularly how molecular events and adaptations to genetic or environmental vulnerabilities result in maladaptive communication within and between regions of the brain that regulate behavior.

All of the authors whose articles are compiled here endeavor to envision a future in which this knowledge has been used to develop successful therapies. It is our hope that this vision will spark new investigative directions for neurobiologists as well as provide clinicians with a sense of the emerging medications and treatments that will shape the future of their practice.

Importantly, we wish to thank the Hot Topics' editor, Dr Bita Moghaddam, whose keen insight into the field of neuropsychopharmacology has provided a compendium of outstanding perspective articles that highlight many of the most exciting findings and scientific viewpoints from the last year. We would also like to thank the ACNP, embodied by Diane Drexler, and Nature Publishing, by Elizabeth Durzy, for their untiring devotion to this project and its demanding timeline.

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