Modulators of Glutamatergic Signaling as Potential Treatments for Neuropsychiatric Disorders

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This book opens a new chapter in neuropsychopharmacology. It provides with a comprehensive review of the glutamatergic system and its involvement in multiple disorders of the central nervous system.

For more than five decades, the focus on monoamines transmitters helped the development of multiple therapies for neurological and psychiatric disorders. The glutamatergic system is much more complex and has the potential to offer novel approaches to help patients. A plethora of evidence, in preclinical and clinical research, support the involvement of glutamate in most disorders of the central nervous system.

Multiple research studies have been conducted to evaluate the effect of different drugs and new molecular entities on various psychiatric disorders. Existing therapies with an effect on the glutamatergic system showed some promising results indicating their potential benefit on different symptom domains such as apathy, avolition and anhedonia. However, more recent research posed additional challenges. A “soft” enhancement of glutamatergic transmission through the blockade of glycine transporters did not lead to a consistent therapeutic benefit in schizophrenia, substance abuse and OCD. However, some beneficial effects were observed on specific symptom domains such as motivation. Modulators of mGLUR5 receptors showed a beneficial effect in patients with major depressive disorders with inadequate response to SSRIs and SNRIs. If these effects are confirmed, research focused on symptom domains rather than diagnoses will help adequately evaluate the potential benefit of novel therapies involving the glutamatergic system.

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