

Editorial

The health burden of psychiatric disorders is rapidly increasing, whilst the range of available pharmacotherapies is limited and suboptimal with regard to efficacy and tolerability. Recent findings support a major role for neuropeptides in several of these conditions and thereby identify neuropeptide systems as potential novel therapeutic targets for the treatment of psychiatric disorders. In preclinical models, pharmacological and/or genetic manipulation of corticotropin-releasing factor (CRF), vasopressin, neuropeptide Y (NPY), galanin, bombesin, nociceptin and neurotensin alters anxiety-, depression- or schizophrenia-related responses. Recently, specific and highly potent small molecule neuropeptide receptor agonists and antagonists have been developed that can readily cross the blood-brain barrier. Clinical assessment of several compounds is currently underway. This issue will provide an overview of recent developments in this rapidly advancing field.

The introductory paper by Catherine Belzung and colleagues [1] describes general features of neuropeptides, including the history of their discovery, their definition, classification, biosynthesis, transport, release, inactivation, as well as their interaction with specific neuronal receptors. It focuses more particularly on the involvement of neuropeptides in depression, and anxiety disorders.

CRF is undoubtedly the most extensively studied neuropeptide, notably because of its well-known involvement in the regulation of the hypothalamo-pituitary-adrenal (HPA) stress axis, whose dysfunctioning has been directly linked to the development of stress-related disorders. Thomas Steckler and Frank Dautzenberg give a comprehensive update on the involvement of CRF and its receptor subtypes in affective disorders and drug abuse [2].

Since vasopressin has been shown to be critical for adaptation of the HPA axis during stress through its ability to potentiate the stimulatory effect of CRF, it has been hypothesized that this peptide may provide a good opportunity for pharmacological treatment of stress-related disorders. The availability of the first orally active non-peptide V_{1b} receptor antagonist, SSR149415, opened a new era for examining the role of vasopressin in stress-related disorders. Rainer Landgraf in his review [3] elegantly demonstrates that the capability of vasopressin to respond to both stressful stimuli and mediate genetic polymorphisms makes the central release of this peptide a key process for converging behavioral regulation related to stress disorders.

Christina Carjaval and colleagues [4] review recent developments on the role of NPY in emotion and alcohol dependence and they examine the potential of the NPY system as a novel therapeutic strategy in the treatment of anxiety, depression and alcohol-related disorders.

Although less studied within the CNS field than the previous peptides, gastrin-releasing peptides and their receptors are increasingly examined for their involvement in psychiatric and neurological diseases. Rafael Roesler and his colleagues [5] review this emerging idea.

Becky Kinkead and Charles Nemeroff [6] discuss the idea that neurotensin receptor ligands may represent an innovative approach for the treatment of schizophrenia.

There is now compelling evidence that the orphanin FQ/nociceptin (OFQ/N) system may represent a valuable target for the development of drugs treating a variety of psychiatric disorders. Rainer Reinscheid [7] discusses the recent development of OFQ/N ligands and their behavioral effects in animal studies.

Our understanding of the role of the galanin system in modulating emotional behavior and drug withdrawal has progressed in recent years. Andrew Holmes and Marina Picciotto [8] summarize in their review current developments and scientific achievements that have been made to elucidate the functions of galanin in psychiatric disorders.

In the last review article, Michael Cowen and Andrew Lawrence [9] discuss the potential of therapeutic strategies targeting neuropeptide systems implicated in aberrant alcohol-seeking behaviour.

The search for novel treatment strategies for psychiatric disorders is driven by the growing medical need to enhance the response rate, efficacy and side-effect profile of existing drugs. Given the wealth of animal and human data supporting the role for neuropeptides in modulating behavioral responses, targeting these systems remains a highly promising avenue for the development of novel clinical entities in psychiatric disorders.

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