BJP British Journal of Pharmacology

DOI:10.1111/bph.12474
www.brjpharmacol.org

Themed Section: Neuropeptides

EDITORIAL

The background to this themed issue on neuropeptides

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Keywords
CGRP; GPCR; motilin; neuropeptides; pituitary adenylyl cyclase-activating peptide; substance P; TRPV1; vasoactive intestinal peptide

A meeting of the *British Pharmacological Society* in association with the European Neuropeptide Club and Americal Summer Neuropeptide Conference in June 2012 led to this themed issue on neuropetides. A wide range of neuropeptides are discussed, in various physiological and pathophysiological conditions, with respect to their upstream and downstream pathways. It is clear, at this point in time, that targeting neuropeptides has therapeutic potential in pathologies ranging from migraine to obesity. It is also clear from the reviews in this issue of the *British Journal of Pharmacology* that there is still so much to learn.

LINKED ARTICLES
This article is part of a themed section on Neuropeptides. To view the other articles in this section visit http://dx.doi.org/10.1111/bph.2013.170.issue-7

The inspiration for this themed issue on neuropeptides stemmed a *British Pharmacological Society* (BPS) Focused Meeting on Neuropeptides in June 2012, held in association with the European Neuropeptide Club and American Summer Neuropeptide Conference. This was the first time that all three organizers had jointly held a meeting and it was a resounding success, attracting many eminent neuropeptide researchers from around the world. The meeting was further inspired by its location at King's College London, just prior to the London 2012 Games, providing a prime time for scientists to join in London for a scientific event. On the administrative side, the BPS enabled the meeting to flow smoothly from beginning to end. Meanwhile, the local organizers, Professors Sue Brain and Helen Cox, did a wonderful job of developing the content of the meeting, supported by an international advisory panel, including Professors Erika Pinter, Barbara Kofler, Illana Gozes, Piero Geppetti and Dr David Poyner. Aside from symposia addressing neuropeptides and their receptors directly, sessions were also focused on receptors upstream of neuropeptide release, in particular TRPV1 and TRPA1. Invitations to invited speakers to submit review articles on the subject area relating to their talk has resulted in this themed issue, containing reviews on a wide array of neuropeptide and TRP-related subjects ranging from the role of neuropeptides in obesity to the role of proteolysis in GPCR function and beyond.

Summary of content

This special edition comprises 7 reviews, covering neuropeptides and both their upstream and downstream receptors. Bodkin and Fernandes (2013) discuss the protective role of TRPV1 in sepsis and the downstream neuropeptide, substance P. Over recent years, TRPV1 has increasingly been shown to exhibit paradoxical effects in inflammation and this review captures the intriguing protective effect of TRPV1 in sepsis, as well as evidence for an anti-inflammatory role for substance P in this disease. In contrast, calcitonin gene-related peptide (CGRP), predominantly colocalized in sensory neurons with substance P, has been implicated in the pathophysiology of migraine, but in this case, the neuropeptide plays a detrimental role. Thus, CGRP receptor antagonism has offered a promising therapeutic target for the treatment of this condition, although no CGRP antagonist has yet been approved for the treatment of migraine, principally because of liver toxicity, but possibly also because more than one CGRP-responsive receptor underlies migraine

pathophysiology (Walker and Hay, 2013). A better understanding of the structure-activity relationship of CGRP with its receptors may prove crucial in the development of future CGRP antagonists as well as selective agonists, crucial for increasing our knowledge of this neuropeptide's actions (Watkins *et al.*, 2013).

As well as therapeutic antagonists, neuropeptide receptor agonists may also have therapeutic potential. Sanger *et al.* (2013) discuss the beneficial effects of the galanin relative, motilin. Indeed, new non-molitide, small molecule receptor agonists are entering clinical trials for the treatment of patients undergoing enteral feeding and those suffering from diabetic gastroparesis. Furthermore, vasoactive intestinal peptide and pituitary adenylyl cyclase-activating peptide have been shown to exhibit neuroprotective and immodulatory effects, as discussed by Waschek (2013). Receptors for these neuropeptides may be effective targets for the treatment of neurodegenerative and neuroinflammatory diseases, such as Alzheimer's disease and multiple sclerosis. In obesity, the role of neuropeptides is particularly complex with multiple orexigenic and anorectic neuropeptides playing a role (Boughton and Murphy, 2013). The complexity of the homeostasis in body weight is described by the authors, suggesting that combinations of neuropeptide-targeted therapies may be the future of obesity therapeutics.

Finally, therapeutically targeting of neuropeptides is not necessarily limited to pharmacological modulation by receptor agonists and antagonists. Peptidases play in an integral role in the actions of neuropeptides, acting via GPCRs. As discussed by Cottrell (2013), it has long been known that peptidases regulate GPCR activation by modulating bioactive peptides, and that many GPCRs are degraded by peptidases in lysosomes. However, the authors discuss more recent findings that proteolysis also regulates other aspects of GPCR activity, including their transport through the endocytic system and signalling from endosomes. Thus, the pharmacological modulation of peptidase activity has a massive potential to affect neuropeptide function and selective inhibitors of peptidase subtypes allows for specific effects. It will be interesting to see how this compares to the use of agonists and antagonists in future.

Concluding remarks

This themed edition captures just a snapshot of current neuropeptide-related research and apologies for not being able to cover more neuropeptides and more diseases. However, we hope that the review articles in this edition provide enjoyable reading and that it will stimulate future publication of neuropeptide-related research in this journal. There is still so much to learn.

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