



Centre for Integrative Physiology

Research Briefings

Are Neuropeptides Brain Hormones?

NEURONS USE MANY DIFFERENT CHEMICAL SIGNALS TO COMMUNICATE INFORMATION, INCLUDING MORE THAN 100 DIFFERENT PEPTIDES. MANY OF THESE NEUROPEPTIDES EVOKE SPECIFIC AND COHERENT BEHAVIOURS AND HAVE BEEN LINKED TO A NUMBER OF NEUROLOGICAL DISORDERS. INCREASINGLY, WE ARE RECOGNISING THAT PEPTIDE SIGNALS PLAY A ROLE IN INFORMATION PROCESSING THAT IS QUITE UNLIKE THAT OF CONVENTIONAL NEUROTRANSMITTERS.

NEUROTRANSMITTERS VERSUS NEUROPEPTIDES

Neuropeptides are a large and important class of messenger molecules that carry information between neurons in the brain. There are at least 100 different neuropeptides in the mammalian brain, and most of these are made in and released from the hypothalamus. Some are released into the blood, with peripheral effects as endocrine hormones. Of these, the magnocellular vasopressin and oxytocin neurons have proved to be a good model system for revealing important aspects of many neuronal functions, including neuropeptide release. The classical way that neurons communicate with each other is by neurotransmitter molecules that are packaged in small vesicles that are released at synapses between neurons. However, neuropeptides are packaged separately from neurotransmitters, and are released by different mechanisms from many parts of a

neuron, including nerve endings, somata and dendrites. Indeed, typically 85% of the peptide content is in the dendrites. The release mechanisms for dendritic neuropeptide release can be very different from axon terminal release, and for vasopressin and oxytocin, differentially regulated release allows peptide effects in the body to be independent from peptide effects in the brain.

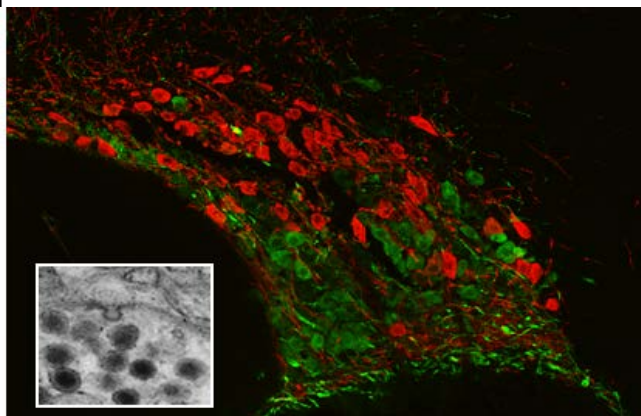
SECRET MESSAGE VERSUS PUBLIC ANNOUNCEMENT

Neuropeptides usually interact with G protein-coupled receptors to activate intrasignalling pathways that can affect many different aspects of cells. Neuropeptides often act back on their cells of origin, for example to facilitate the development of patterned electrical activity. They can also act on their neighbours to bind the collective activity of a neural population into a coherent signalling entity. Finally, the co-ordinated population output can transmit

waves of peptide secretion that act as a patterned hormonal analogue signal within the brain. At their distant targets, peptides can re-programme neural networks, by effects on gene expression, synaptogenesis, and by

Mike Ludwig, PhD
Professor of
Neurophysiology

Tel: +44 (0)131 650 3275
Email: mike.ludwig@ed.ac.uk



functionally rewiring connections by priming activity-dependent release. Classical neurotransmitters pass “whispered secrets” from one particular cell to another; they carry a message that matters only at a particular time and a particular place. By contrast, neuropeptides are “public announcements”, the messages endure, at least for a while; they are messages not from one cell to another, but from one population of neurones to another – these are hormone-like signals.

PRIMING OF RELEASE

In the hypothalamus, large amounts of oxytocin and vasopressin are released from neuronal dendrites independently of release from nerve terminals. Dendritic peptide release can be modulated by *priming*. Priming involves making vesicles readily available for subsequent activity-dependent release, thus enhancing the capacity for the local interactions that co-ordinate neuronal activity. By enhancing intercommunication, peptides can “reprogram” the behaviour of a neuronal system. Peptides might also prime target areas within the brain which harbour their receptors, triggering a cascade of temporary functional reorganisation of the neuronal networks, providing the

substrate for prolonged behavioural effects.

NEUROPEPTIDES AND BEHAVIOUR

Many different peptides evoke specific effects on behaviour. For example, oxytocin is involved in social behaviours, including bonding and maternal behaviour, and vasopressin acts in the brain to affect social recognition and aggression. Other nerve cells release other peptides and they have effects on other emotions and behaviours.

Evidence of the hormonal nature of the behaviour effects of peptides comes from experiments involving gene manipulation, either through transgenic mutations or viral gene transfer, showing that behavioural traits accompany alterations in the distribution of peptide receptor expression. Thus, it appears that it is not the distribution of fibres of peptidergic neurons in the brain that determines particular behaviours, but the distribution of the peptide receptors.

It is now time to bridge the insights emerging from studies of social cognition and social behaviour in animals to human research. Vasopressin and oxytocin have been linked to human neurological disorders such as social anxiety

disorder, depression, schizophrenia and autism spectrum disorder. In addition, disorders of appetite regulation, libido, and mood are among many potential targets of peptide-based therapies. In the future, ‘sniffing’ neuropeptide analogues (intranasal administration) may open a gateway to the brain, and diffusion of the peptides to its receptor sites may be an alternative way for treatment of some of these disorders.

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