Innervation of urocortinergic neurons in the Edinger-Westphal nucleus in the rat

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Urocortinergic neurons in the Edinger-Westphal nucleus (E-WN) play a decisive role in adaptation to stress. These neurons mount a robust immediate early gene response to acute stress, and exhibit no habituation upon chronic exposure to stressful stimuli. Interestingly, however, urocortin mRNA is clearly down-regulated under conditions of chronically elevated levels corticotropin-releasing factor (CRF). Although an increasing body of knowledge is available on the physiology of E-WN urocortin neurons, little is known about their afferent connections. Here we will report interactions between urocortin cells and terminals immunoreactive to serotonin, CRF and Met-enkephalin in the E-WN and in the rostral dorsal raphe nucleus (rDR).

Dense networks of serotoninergic and CRF-positive fibres were found in the caudal E-WN and rDR, whereas enkephalinergic fibres were scattered throughout the whole E-WN area. With double-immunolabeling close appositions were seen between urocortinergic neurons and fibre terminals immunoreactive to CRF, serotonin and enkephalin. Axon terminals positive to these compounds were not only juxtaposed to Ucn perikarya, but also to their primary dendrites. The ongoing electron microscopic studies have to confirm the presence of synaptic connections.

The role of Ucn in stress adaptation is clear, and the potential involvement of Ucn in stress-related disorders has been hypothesised. Intriguingly, CRF, serotonin and opioid peptides all play a part in biological responses to stress, and they may also contribute to stress-induced pathologies. CRF type 2 receptor, serotonin 1A receptor and opioid receptors are all present in the E-WN. However, further studies are needed to identify the existence of these receptors on Ucn neurons. This study provides morphological evidence for interactions between stress-sensitive systems in the rat midbrain. Furthermore, our results will further help elucidating stress regulatory neuronal circuits, and improve our understanding of the role of interactions between these compounds in stress adaptation.

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