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The finding reported by Dr T. M. Jessell of the presence of certain glycolipid stage-specific embryonic antigens on subpopulations of rat dorsal root ganglion cells very probably represents a property of the sensory neuron and is not causally related to the presence of certain neuropeptides in these nerve cells. This is illustrated by the fact that, although all dorsal root ganglion cells containing somatostatin-like immunoreactivity express a glycolipid on their surface, this antigen is not found on central nervous system cells containing somatostatin-like immunoreactivity. In discussion it was suggested that it would be interesting to investigate the effects of neonatal capsaicin treatment on the presence of the glycolipid determinants.

The electrophysiological effects of neuropeptides on the dorsal horn of the spinal cord are incompatible with a role as fast excitatory neurotransmitters. As is the case of sympathetic ganglia they probably produce changes in neuronal excitability that are of slow onset and long duration. Adenosine triphosphate appears to be a candidate as a fast neurotransmitter used by at least some dorsal root ganglion cells, as indicated by the fact that it produces excitatory effects and that its stable analogues have a similar action. However, by analogy with other neurotransmitter systems, it remains possible that it is co-released with other transmitters. The availability of potent and specific receptor antagonists would allow its postulated role to be established more firmly. It was emphasized in discussion that the relation between adenosine triphosphate and the presence of the enzyme fluoride-resistant acid phosphatase in a substantial proportion of small dorsal root ganglion cells remains largely unknown; it is complicated by the fact that the enzyme is only found in dorsal root ganglion cells of certain species of rodents. However, there is evidence for the presence of different forms of the enzyme in different mammalian species.

The evidence presented by Dr S. P. Hunt for the existence of peptidergic and non-peptidergic C fibre afferents that project to the same peripheral tissues and convey similar information but project to different areas of the dorsal horn of the spinal cord, raises the question of the functional significance of neuropeptides in sensory systems. In discussion it was pointed out that there is some evidence to indicate that a decrease in substance P-like immunoreactivity and in the activity of fluoride-resistant acid phosphatase is not accompanied by a change in C fibre conduction. This would tend to suggest that at present these substances represent merely biochemical markers. However, by analogy with other regions of the nervous system, it is very difficult to correlate the measurement of static levels of neurotransmitters with function. The presence of various neuropeptides, such as substance P-like immunoreactivity and calcitonin gene-related peptide-like immunoreactivity in nerve fibres in the skin and their marked effects on histamine release from mast cells raises the question of their physiological significance. Morphologically, no clearcut association between substance P-like immunoreactivity and mast cells could be demonstrated in rat skin. However, it could still exist functionally if the substance P-like immunoreactivity were to diffuse over some distance from sites of release. Results obtained in bullfrog sympathetic ganglia have indicated that a luteinizing hormone-releasing hormone-like peptide can diffuse over tens of micrometres before it acts on its target cells.

Detailed morphological and physiological studies on other neuropeptide-containing systems are needed to establish whether such a 'neuroparacrine' mode of action constitutes a general feature of peptidergic neurotransmission.

As emphasized by Professor H. Kosterlitz in his presentation, for opioid peptides, as for classical neurotransmitters, radioligand binding studies must be corroborated by biological assays before the existence of a physiological receptor can be assumed. The existence of at least three receptor subtypes for opioid peptides (named μ, δ and κ) is now well established. The proposed σ sub-type is probably non-opioid, since naloxone does not bind to it. The comparison between receptor subclasses in peripheral and central tissues is complicated by the fact that in the former it relies mainly on bioassay results, whereas in the latter it has been established through radioligand binding assays. Thus, whereas [Met]enkephalin is a better ligand for δ receptors than for μ receptors in peripheral tissues, the autoradiographic distribution pattern of [^{3}H]naloxone binding (quite a selective antagonist at μ sites) follows the immunohistochemical distribution of the central nervous system pro-enkephalin system very closely. This indicates that in these regions the enkephalin system co-distributes with the μ binding sites. This is supported by the fact that the μ receptor agonist morphine exerts an antinociceptive action in these regions. As emphasized by Professor Kosterlitz, the study of the function of endogenous opioid peptides is still in its infancy. The classification of the different receptor subtypes represents an important framework for distinguishing between the multiple actions of endogenous opioid peptides. The development of selective and potent antagonists, mainly for the δ and κ subtypes, represents an important area for future research.

The evidence presented by Dr V. Höllt for the occurrence of a high density of κ opioid binding sites in the spinal cord, but not in the brain, indicates a differential distribution of opiate receptor subtypes in different parts of the central nervous system and may have implications for the role of opioid peptides in analgesia. Interestingly, dynorphins A and B are anti-nociceptive on intrathecal, but not on intraventricular application. In discussion it was stated that morphine is more potent in rats with chronic arthritic pain than in control animals, suggesting that in this animal model the opioid peptide system is not only activated at the level of peptide synthesis, but also at the receptor level. It might be interesting to perform subdissections of the thalamus in order to investigate whether the levels of opioid peptides are affected differentially in animals with chronic arthritis. The general problem of correlating results obtained in *in vitro* studies with *in vivo* effects was raised and it was suggested that such correlations could be the result of non-receptor events, such as metabolism. Although this may be the case for the shorter opioid peptides, it seems an unlikely explanation for the effects of the larger opioid peptides, such as β-endorphin and BAM 22, that are metabolically quite stable following their application *in vivo*.

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