complete clockfaces, so no new distal tissue production. But the double posterior limbs discussed by Slack and Savage were produced not by surgery in the adult, but by operations in the embryo that altered the antero-posterior polarity of the limb-forming tissues. It is known (see Slack, *J. Embryol. exp. Morph.* **39**, 151; 1977) that flank tissue specifies the polarity of the developing forelimb, and by transplanting a strip of flank to the anterior margin of the limb-forming tissue they can produce symmetrical double-posterior limbs. Such limbs would have to possess, on the model, partial, mirror-image duplicated sets of positional values; yet on amputation they frequently regenerate a double-posterior pattern similar to that of their initial development. This is in clear contravention of the complete circle rule.

French *et al.* do suggest, in the initial *Science* paper, how the apparent evidence that organ rudiments are successively polarised in two Cartesian-type axes during early development (see the above Slack articles and for example Harrison, *J. exp. Zool.* **32**, 1; 1921), may be reconciled with later regeneration behaviour of limbs initially developing mirror image symmetry in embryonic life, and indeed the possibility of stable initial development of such limbs at all, remains a severe challenge to the clockface model. Perhaps we should not expect to understand, in one breath as it were, the initial genesis of patterns in growing fields in embryos and then their later capacities in regeneration (if they show such capacities, which of course the limbs of higher vertebrates do not). □

Ubiquitous neuronal peptides

from John Hughes and Leslie Iversen

The 1978 Winterschool of the European Training Programme in Brain and Behaviour Research was held on January 8-14, at Zuoz, Switzerland on the topic 'Neuronal Peptides'. The Chairman was J. J. Dreifuss, Geneva.

DURING the symposium, participants attempted to come to terms with the avalanche of new data that threatens to overwhelm those involved in this field. At the latest count, at least 20 peptides are known in mammalian brain with distributions and properties compatible with neurotransmitter functions.

The widespread and often unexpected distribution of neuronal peptides has been demonstrated recently in several laboratories. F. Vandesande (University of Ghent) illustrated the powerful resolution available with immunohistochemical staining techniques. By using carefully purified antisera it is possible to stain selectively hypothalamic neurones containing the closely-related pituitary peptides oxytocin and vasopressin. Furthermore, some vasopressin neurones seem to exist within extrahypothalamic areas of brain. Similarly, B. Flerko (Pécs) described the existence of the hypothalamic releasing hormone LHRH in neurones in various extrahypothalamic areas, and M. Palkovits (Budapest) provided radioimmunoassay results from microdissected brain regions supporting the existence of this and other hypothalamic releasing hormones outside the hypothalamus. Unpublished results of Lundberg and Hökfelt (University of Stockholm) indicate the presence of nerve fibres in the cervical vagus containing substance P, enkephalins, gastrin, somatostatin and vasoactive intestinal peptide (VIP). The nodose ganglion contains VIP and somatostatin-containing cell bodies and these together with substance P cells presumably form part of an afferent system, whereas enkephalin and gastrin seem to be contained in efferent fibres originating from cells within the brain. Equally intriguing is the possible coexistence of somatostatin and noradrenaline in some sympathetic ganglion cells (Hökfelt *et al. Proc. natn. Acad. Sci. U.S.A.*, **74**, 3587; 1977). The coexistence of more than one putative transmitter within a neurone clearly has important implications for generally accepted concepts regarding the release and action of neurotransmitters.

J. Hughes (Imperial College, London) described studies on the biosynthesis of the enkephalins, suggesting the need for ribosomal synthesis and the probable existence of a larger polypeptide precursor. There is evidence that a single large polypeptide may represent the common precursor for ACTH and β-lipotropin in the pituitary, and the latter peptide can in turn give rise to α-MSH and β-endorphin. There are other examples of families of peptides originating from a common precursor. Thus, radioimmunoassay results suggest the presence of both cholecystokinin (CCK) and its carboxy terminal octapeptide (CCK-8) in the brain (Dockray *Nature* **262**, 92; 1976; Muller *et al.*, *Proc. natn. Acad. Sci. U.S.A.*, **74**, 3035; 1977). The cerebral cortex is particularly rich in these peptides, which is of interest since this area is relatively sparsely innervated by other known peptidergic systems. Gastrin and CCK probably share a common evolutionary precursor (Larsson & Rehfeld *Nature*, **269**, 335; 1977) and it is not surprising that gastrin-like immunoreactivity has also been reported in brain (Vanderhaegen *et al. Nature*, **257**, 604; 1975).

Turning to the possible functions of CNS peptides, J. S. Kelly and L. L. Iversen (MRC Neuropharmacology Unit, Cambridge) discussed the possible involvement of substance P as a primary sensory transmitter involved in the transmission of pain, and the interaction of enkephalin-containing neurones with pain-transmitting mechanisms at the spinal cord and brain stem level as a possible 'gating' mechanism (P. Wall, University College, London). R. F. Schmidt (Kiel) described the various chemical mechanisms involved in activating and sensitising pain fibres in the periphery. A special category of muscle afferents responds to painful stimuli and to pain-inducing chemicals such as 5-hydroxytryptamine or the peptide bradykinin. The action of bradykinin may involve a prostaglandin intermediate, since its effects on pain fibres are blocked by aspirin.

J. Fitzsimmons (University of Cambridge) reviewed the remarkable CNS effects of angiotensin II in eliciting drinking behaviour in most vertebrates. An outstanding question here is whether such effects are normally elicited by the circulating peptide acting on targets in the brain lying outside the blood–brain barrier, or whether an intrinsic CNS renin/angiotensin system is involved. T. B. van Wimersma Griedanus (University of Utrecht) described results obtained with D. de Wied showing that ACTH fragments and particularly vasopressin are able to delay the extinction of learned behaviour in animals. Whether the central actions of vasopressin are related to an intrinsic system of neurones containing this peptide in brain, or whether the pituitary vasopressin system is involved is again unclear.

The Winterschool showed that the field of neuronal peptides remains a rapid growth area; many unanswered questions have been raised by the sudden discovery of this large group of new putative chemical messengers in the brain, and there will certainly be more surprises to come. □

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0028–0836/78/0271—0769$01.00