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Editorial
The Brain's Opium
(Human Beta-endorphin)

In recent years, it has become evident that peptides of relatively small molecular weight play an important role not only in the regulation of endocrine function but also in the control of certain pathways in the central nervous system.

Present evidence indicates there are two independent peptidergic systems; one is characterized by the presence of the short chain peptides, methionine-enkephalin and leucine-enkephalin and is widespread throughout the central and peripheral nervous systems (Hughes **et al.,** 1977; Simantov **et al.,** 1977) whereas the other system contains the long chain peptide, beta-endorphin and is centred around the hypothalamus-pituitary axis with extensions into the thalamus, midbrain, medulla and pons (Rossier **et al.,** 1977).

The idea that the brain produces an "endogenous analgesic" is based in part on the variation in our perception of pain in different circumstances. Indeed, pain perception may be completely suppressed for a while, as may occur with war wounds. Possibly, too, stimulation of the release of such a substance within the central nervous system by acupunture might be the basis for the relief of pain this treatment can provide.

The human brain contains receptors which will bind opium specifically. Normally these receptors probably modulate pain perception by reacting with a natural brain substance; only coincidentally do they bind the active principle of the opium poppy, which therefore acquires analgesic properties. Chronic opiate abuse would be expected to cause sustained suppression of the endogenous analgesic; so that suddenly depriving an addict of opiates would lead to receptors being unoccupied

and the features of opiate withdrawal. Indeed, if acupunture does stimulate the release of the "natural opiate" then it would explain the reported success of electroacupunture in treating the symptoms of heroin withdrawal. All these ideas, however, have remained speculative.

These substances, the enkephalins, each contains five amino-acids and differ from each other only by one amino-acid. Soon after their discovery the structure of one of the enkephalins was noted to be identical with part of a much larger pituitary peptide hormone called beta-lipotrophin (-LPH); and subsequently other peptides related to -LPH, the endorphins, have been shown to have even greater affinities for the opiate receptors. One of these, beta-endorphin, is at least 30 times more potent than enkephalin in its binding to opiate receptors and is a more powerful analgesic.

Beta-lipotrophin is found in the anterior pituitary in the same cells as corticotrophin (ACTH) and is secreted in parallel with it under both physiological and pathological conditions, yet its biological role has remained unknown. Recent studies suggest, however, that -LPH may be the precursor of the endorphins, the family of endogenous analgesics. We might expect that beta-endorphin would be secreted during stress along with ACTH.

After removal of the pituitary in animals, opiate agonist activity can still be found in brain tissue; this material resembles beta-endorphin. Some authors have reported the presence of -LPH and ACTH in the brains of several species independent of the presence of the pituitary and suggested that their distribution may be dissociated. Others have found beta-endorphin in the cerebral fluid of patients with no LPH or ACTH in their blood owing to pituitary or hypothalamic disease. Hence these peptides may be synthesized directly in the brain instead of exclusively in the pituitary, as has been assumed.

The physiological roles of brain ACTH, -LPH, and beta-endorphin are likely to be different from their counterparts derived from the pituitary: they may, indeed, have to be considered more as neuro-

transmitters and behaviour modulators than as hormones. Like morphine, enkephalin and beta-endorphin act on hypothalamic mechanisms to cause the release of both growth hormone and prolactin in rats, and an analogue of enkephalin has now been shown to have the same hormonal effects in man and in addition to lower gonadotrophin and ACTH concentrations.

Immediate priorities in endorphin and enkephalin research may lie, then, not so much in attempts to study their alterations in the blood but instead in careful chemical and pharmacological characterization of these substances in the brain and CSF. Studies along these lines may indicate the true physiological role of these peptides and their relation to pain perception and behaviour.

These substances, apart from their analgesic actions, have their effects on respiration, mood, gastro-intestinal motility and endocrine functions. At present, it is not possible to allocate different physiological roles to the different types of receptors (Kosterlitz, 1979). The discovery of these substances has envisaged a new approach to the study and management of drug dependence and psychosis but the results of their use in such disorders are still controversial.

Ahmed Okasha

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EDITORIAL

The Evolutionary Value of Tolerance of Depression in Modern Life

The term depression is getting to be more and more mutilated through the abuse of psychiatrists. Instead of stimulating empathy, sympathy, care, and responsibility it has become a conditioned stimulus to swallowing tofranil, ludiomil, tryptizol, parnate etc... As much as the homosapiens is especially characterized by symbolic thinking, language, awareness, and free choice he is particularly characterized by depression.

The psychiatrist, as well as the layman, has to revise the real meaning of the word before submitting to the creeping invasion of psychiatric terminology on human emotions. This warning should not be taken as an antipsychiatric cry or an attitude of nihilism towards drug therapy; on the contrary, it should stimulate thinking in other terms that are more representative of pathology, with the aim of manipulating ourselves and our patients in a better way.

Any clinical artist is familar with many types of depression other than those forced upon his mind through the current shortcomings of scientific language. Any honest reviewer of drug research on depression will find himself lacking an essential dimension in what is written on the "pills of happiness", and how the resolution of this human tragedy is established through mysterious orange, yellow, or red tablets administered t.d.s. This lacking dimension is not simply the poetic touch of the misery of our life but is mostly the profound biological meaning of depression. In the DMP I (The Egyptian Manual of Psychiatric Disorders, 1975), there are 11 types of depression including depressive personality and reactive neurotic and psychotic types. In the DSM II there are 7 types, in the ICD 8 there are 8 and in the DSM III there are 9 types (other than reduplications on various axes). All such types are mainly descriptive with little or no reference to meaning, function, goal, value, or corresponding management.