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Opioid Receptors and Mood

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Opioid drugs, typified by morphine, produce their pharmacological actions, including analgesia, by acting on receptors located on neuronal cell membranes. Neurons are made up of nerve ending or axon (presynaptic), a gap (synapse), and a target cell where the receptor resides (postsynaptic). The opioids have their effect at the presynaptic end of the nerve junction and act to inhibit the release of the neurotransmitter. This action is the major effect of the opiates on the nervous system.

Opioid drugs hijack a complex neuromodulator system composed of three receptors, mu, delta and kappa, which interact with a family of endogenous opioid peptides known as β-endorphin, enkephalins and dynorphins. Opioid receptors form a subfamily of G-protein coupled receptors, which also includes the non-opioid nociceptin/orphanin FQ receptor. Both receptors and peptides are expressed throughout peripheral and central nervous systems, and have been the subject of intense investigations. Opioids play a central role in pain processing and regulate many other aspects of physiology, such as stress responses, respiration, and gastrointestinal transit, in addition to endocrine and immune functions. The mood-regulating properties of endogenous opioids represent another main aspect of opioid physiology. The potent euphoric effects of known opioid drugs like heroin, and the high density of peptides and receptors in limbic brain areas, set the opioid system as a central player in both reward processing and mood control, and a feasible target to treat emotional dysfunction.

Today, opioids are beginning to be considered for the treatment of major diseases of depression (MDD). Agonists such as buprenorphine are used in the specific contexts of hard or impossible to manage depression (refractory depression) and depression-addiction comorbidity, and may have broader indications. In summary, kappa (dynorphin) agonists and delta (enkephalin) antagonists have promising antidepressant potential, and both dynorphin and kappa drugs are under development. In contrast, data from mu (endorphin) analysis appear more complex. Endorphins, enkephalins and dynorphin appear as important and highly distinct players in the regulation of emotional states. Animal studies show that dynorphin improves mood states acutely, enkephalins decrease mood after stress, and endorphins exert contrasting effects on mood. In the future we will no doubt see a whole new class of antidepressants based on the regulation of the opioid neurotransmitters. The clinical implications of this area of research will help clinicians in addiction treatment to better understand the behavior of clients. Those treated are deserving of an empathic treatment based on a better understanding of the neurochemistry which their brains have been subjected to.

Receptor	Function
delta (δ)	analgesia, antidepressant effects, convulsant effects, physical dependence, modulate μ-opioid receptor-mediated respiratory depression
kappa (κ)	analgesia, anticonvulsant effects, depression, dissociative/hallucinogenic effects, diuresis, dysphoria, miosis, neuroprotection, sedation, stress
mu (μ)	analgesia, physical dependence, respiratory depression, miosis, euphoria, reduced GI motility, physical dependence, possible vasodilation
Nociceptin	anxiety, depression, appetite, development of tolerance to μ-opioid agonists
zeta (ζ)	tissue growth, embryonic development, regulation of cancer cell proliferation