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Endorphin: function and mechanism of action

Ansam Hussein Ali¹, Hanan Shihab Ahmed¹, Alyaa Salih Jawad¹, Mohammed Ahmed Mustafa²

¹Department of Immediate Aid, Northern Institute University-Al -Dour Institute Technical

²Department of Medical Laboratory Techniques, College of Technology, University of Imam Jafar Al-Sadiq Dujail

*Corresponding author: *mohammed.alsad3@ gmail.com

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Abstract

Endorphins are chemicals naturally produced by the nervous system to manage pain or stress. They are often called “feel-good” chemicals because they act as a pain reliever and happiness booster. The exact mechanism of endorphins can be perceived through development in the peripheral nervous system (PNS) and the CNS through two distinct features. The illusion of pain relief in the PNS is produced by beta-endorphins that bind to opioid receptors. In the CNS, mu-opioid receptors are more abundant in descending pain control circuits including the amygdala, mesencephalic reticular formation, periaqueductal gray matter (PAG), and rostral ventral medulla. As for the Endorphins functions, they are found in high concentrations in certain regions of the brain that help in the transmission of pain sensations, breathing, motor activity, secretion of pituitary hormones, and mood. The relationship between the secretion of endorphins and the stimulating adrenal cortex hormone came through behavioral studies that indicated that stress increases the concentrations of endorphins in the blood and brain. With parallel changes in the pain threshold. Histochemical studies suggest that opiates have important relationships with cells that contain noradrenaline and cells that contain dopamine.

Keywords Endorphins, pain, hormones, periaqueductal gray matter (PAG), and rostral ventral medulla.

Introduction

Endorphins are chemicals naturally produced by the nervous system to manage pain or stress. They are often called “feel-good” chemicals because they act as a pain reliever and happiness booster (Berry, 2018). They are produced in the pituitary gland and deposited there. As compared to a particular chemical formulation, the designation of molecules as endorphins are reliant on their pharmacological effect. Endorphin consists of α -endorphin, β -endorphin, and γ -endorphin. All three preferentially bind to μ -opioid receptors (Li et al., 2012).

Endogenous morphine, coined from the transition into endorphins of the two specific terms, is opioid neuropeptides that are spontaneously formed in the body, having a primary role as an agent that prevents the sense of pain and is also present in cases of enjoyment. Historically, before the discovery and recognition of endorphins, morphine receptors were located in the nervous system. This natural receptor explored the idea that endorphins may occur and have an

effect, which was recently revealed. (Adeodu et al., 2012; Olson et al., 2017).

Endorphins have been found to not only show roles in the central nervous system as neurotransmitters but also as peptide hormones produced by the pituitary gland into the circulatory system. Endorphins are psychologically associated with cases of behavioral disorders such as autism, addiction, and depersonalization disorder, as well as behaviors such as humor and vigorous aerobic activity (Shenoy & Lui, 2018). Since the first two pentapeptides were isolated from the brain, more opioid peptides have been identified in the brain. The two peptides, methionine-enkephalin (Met-ENK) and leucine-enkephalin (Leu-ENK) are known to have potent opiate agonist activities. Using radioimmunoassay and immunocytochemistry it was possible to demonstrate that these peptides are present in the striatum. The striatum is a part of the brain under the cerebral cortex inside the forebrain which receives input from the cerebral cortex and is the main input to the basal ganglia system. Endorphins are the body's

very own natural analgesics or painkillers. They are released during times of stress and pain. They also rush forth during strenuous exercise, often causing a wave of pleasure to come over the individual. This is why exercise feels to many like a good stress release and puts a person in a good mood. Endorphins in the brain work similarly to opium-based drugs, like morphine (Bali et al., 2014).

Synthesis

Beta-endorphins are primarily synthesized and stored in the anterior pituitary gland from their precursor protein proopiomelanocortin (POMC). However, recent studies suggest cells of the immune system are also capable of beta-endorphin synthesis because immune cells possess mRNA transcripts for POMC3 and T-lymphocytes, B-lymphocytes, monocytes, and macrophages were revealed to contain endorphins during inflammation. POMC is a large protein that is cleaved into smaller proteins such as beta-endorphin, alpha-melanocyte-stimulating hormone (MSH), adrenocorticotropin (ACTH), and others. The pituitary gland synthesizes POMC in response to the signal from the hypothalamus; that signal being corticotropin-releasing hormone (CRH). The hypothalamus releases CRH in response to physiologic stressors such as pain, as in the postoperative period. When the protein products of POMC cleavage accumulate in excess, they turn hypothalamic CRH production off – that is, feedback inhibition occurs (Sprouse-Blum et al., 2010; Mousa et al., 2004)

Mechanisms of action of endorphins

Endorphins are released from the irritation of many nerve cells in the CNS. Endorphins inhibit self-responding cells in the cerebral cortex, brain stem, and thalamus. In the hippocampus, pyramidal cells are usually irritated and are also sensitive to naloxone (Rodriguez & Covenas, 2011). Opioid receptors are concentrated in some nerve fibers before the synapses, therefore, endorphins may reduce the release of dopamine and other neurotransmitters by affecting these receptors. Therefore, one of the primary functions of endorphins is to mediate pre-synaptic depression in the CNS. The effects of pre-synaptic endorphins on the activity of neurons may lead to inhibition or irritation of neurons, depending on whether the pre-synaptic neurons are inhibitory or irritating to other neurons. Opioid receptors are divided into groups, depending on pharmacokinetic and biochemical methods. Three groups of live opioid receptors were observed: Delta, Mu, and GABA, which differed in affinity for endorphins as well as in their regions of distribution. The delta receptors have a high affinity for envelopes and are distributed in different regions of the brain in comparison with the mu and GABA receptors (Chaudhry et al., 2020).

Although morphine binds mainly to the mu-receptors, injecting morphine into the blood stimulates the release of the envelopes. Thus, envelopes may contribute to part of the physiological response to morphine, possibly by binding to the delta receptors. And the distribution of these receptors and their different types indicates that they mediate different

physiological activities. The sedative effects of endorphins occur through the mu-receptors, whereas the delta receptors may regulate emotional behavior, the mitotic enkephalin regulates the mu-receptor, and the enkephalin regulates the delta receptors. It appears that the GABA receptors are affected by dinorphine. Therefore, it can be said that opiates exhibit their varied physiological effects by binding them with different types of their receptors. Regardless of the physiological and pharmacological differences of these receptors, binding to these three-third receptors inhibits adenylate cyclase and neutralizes calcium ion channels (Amrita, 2018; Mustafa, et al., 2020).

Mechanism of action

Via operation in the peripheral nervous system (PNS) and the CNS, the endorphin pathway can be seen through two separate lenses. The sensation of pain relief is created in the PNS Beta-endorphins bind to specific receptors for opioids (Shrihari, 2019). Opioid receptors are classified into four major G-protein-coupled receptor classes: mu-receptors, delta-receptors, kappa-receptors, and nociceptin receptors. Between the beta-endorphins and the mu-receptors, there is the largest binding potential. Mu-receptors can be located all over the PNS nerves. Analgesic effects are recognized as this beta-endorphin to mu-receptor binding happens on nerve endings (happening pre-synaptically or post-synaptically). The implications are realized when the foregoing binding results in the activation of chemical events that, among other tachykinins, inhibit the release of substance P, which is an essential undecapeptide in the transmitting of pain. In the peripheral nervous system, and as beta-endorphin to mu-opioid binding appears, it also takes place in the central nervous system. However, there is a distinction, since the process caused by the attachment prevents the activation of the gamma-aminobutyric acid (GABA) inhibitory neurotransmitter as compared to P. With this GABA inhibition, the result is an increase in the development and function of dopamine, the neurotransmitter associated with enjoyment and reward. In the CNS, mu-opioid receptors are most abundant in descending pain control circuits including the amygdala, mesencephalic reticular formation, periaqueductal gray matter (PAG), and rostral ventral medulla.

Physiological functions of endorphins

Endorphins are usually found in high concentrations in regions of the brain that contribute to the transmission of pain sensations, breathing, motor activity, secretion of pituitary hormones, and mood. The relationship between the secretion of endorphins and the stimulating hormone of the adrenal cortex came through behavioral studies that indicated that stress increases the concentrations of endorphins in the blood and brain. With parallel changes in the pain threshold. Histochemical studies suggest that opiates have important relationships with cells that contain noradrenaline and cells that contain dopamine (Shrihari, 2017).

Pain relief

One of the most remarkable effects of endorphins is in the spinal cord, where there are small nerve cells containing enkephalin that connect to the endings of peripheral sensory neurons that relay information about pain to the spinal cord. These sensory neurons contain another peptide known as substance P, and the sites of the P substance are identified in the sensory pain fibers located in the dorsal root ganglia. The highest concentration of it was observed in the dorsal root nerve cells compared with the ventral root nerves (Zhang, 2013). This indicates that Substance P acts as a neurotransmitter, then released from the central ends of the sensory nerve fibers and substance P has an irritating effect on the nerve unit located in the dorsal horn of the spinal cord. Units irritated by substance P are among those irritated by dermatological pain stimuli. Substance P causes an increase in the responses of the units that are sensitive to pain due to pain stimuli. MIT-enkephalin inhibits the release of substance P from the nerve endings of the sensory pain fibers and the effect of this endorphin is opposite Naloxone. The component neurons contain the binding sites of the envelopes. Consequently, the enkephalin-containing neurons in the dorsal horn may inhibit the release of substance P from the sensory neurons of the dorsal root and thus suppress the transmission of pain to the brain. As pain stimuli cause the spinal cord cells to become more active. And acupuncture inhibits this increase in the electrical activity of nerve cells, while the effect of acupuncture is completely negligible when opioid antagonists such as naloxone are used (Mousa et al., 2004; Mustafa, M.A & AL-Samarraie, M.Q .2020).

Endorphins in the core of the adrenal gland

Mostly, stimuli to a stress trigger a nerve response in the core of the adrenal gland. Many types of stress can lead to analgesia, which can be partially suppressed by the administration of naloxone. Large numbers of enkephalin-containing peptides have been observed in mammals. These peptides are stored in the chromophilic granules, and then excreted with catechol amines in response to stimulation. These peptides may be derived from pro-enkephalin by the proteolysis process. One of these peptides is the E peptide, which contains in its composition the Mitotic and Leu Enkephalin sequences. And that this peptide is 30 times more effective than the dead enkephalin. Therefore, researchers suggested that adrenal core envelopes may contribute to pain relief in life-threatening stress situations (Shirhari, 2017).

Regulating the secretion of pituitary hormones

There is evidence that suggested that opioid peptides may play a physiological role in regulating the release of pituitary hormones. For example, higher concentrations of beta-endorphins were observed in the pituitary blood of a monkey species compared to what is found in the peripheral blood. Also, intravenous injection of opioid peptides has resulted from the release of prolactin, somatotropin, vasopressin, and melanocyte-stimulating hormone. On the other hand, opioid

peptides inhibit ovarian follicle-stimulating hormone (FSH) and LH secretion (Sharma & Verma, 2014).

Endorphins role in reproduction

The isotope of the dead enkephalin was observed to inhibit mating behavior in male sexually active rats. And that Naloxone itself stimulates mating behavior in the opioid receptors and prevents this effect. Naloxone itself also stimulates mating behavior in sexually inactive male rats. Detecting the inhibitory function of endorphins on mating behavior. Therefore, we can say that endorphins may be important in regulating sexual behavior (Zhang, 2013).

The effect of physical exertion on the concentration of endorphins in the blood

Endorphins are secreted in response to the moderate-intensity aerobic physical exertion of 20 minutes or more and maybe excreted in the case of less intense physical exertion if the exertion continues for a long time. And during violent physical exertion that only lasts for a short period, such as running short distances or lifting weights, it is not believed that its concentration in the blood changes significantly compared to the state of rest. Many scientists believe that endorphins are responsible for the happy state of high runner's. Despite the great differences in the timing of endorphin secretion between one runner and another, some of them excrete endorphins after about 10 minutes of running, and others it may take 20-30 minutes before they feel the pleasure and happiness resulting from the secretion of endorphins. Finally, there do not seem to be any noticeable differences in the response of endorphins to physical exertion in women compared to men, as indicated by the results of researches that compared males and females in this regard (Shirhari, 2019).

Role of endorphin in happiness

Endorphins or "pain-killing molecules" or "pain relievers" were linked with pleasure states like emotions brought about by love, laughter, sex, and even appetite. Even though functions mainly in blocking pain, they are also a reason for our pleasure feelings and it is for this reason, it is one of the four major hormones of happiness or pleasure hormones. It's believed that the feelings of pleasure persist to make us realize what time we have had that sort of a good experience and also to boost us to go behind that experience so that pleasure associated with the older one can be felt. Also, happiness expressed as laughter or even the expectation of something funny is known to cause the further release of these chemicals (Sharma and Verma, 2014). Clinically, endorphins have been associated with autism, depression, and depersonalization disorder and are physiologically known to be related to activities like laughter and vigorous aerobic exercise (Boecker et al., 2008).

Dysfunctions

It was believed that continuous exposure of Neuroblastoma neurons to opiates in tissue culture initially led to a decrease in the formation of cyclic AMP, and with time they need for opiates increased to reduce the formation of MAP to the primary level when the cells were exposed to the opiates, which means that the cell became resistant to the effects of opiates. There is also evidence to suggest that opioid drugs also show their effects on nervous tissue by stimulating the formation of mono-QQP (Inagaki, 2018). It has been hypothesized that heroin addicts may suffer from a lack of endorphins during a certain period of addiction and that exogenous opioids may inhibit the formation of brain or pituitary endorphins through negative feedback. This leads addicts to develop a true state of endorphin deficiency. Based on the catecholamine theory in schizophrenia, increased dopamine formation and thus increased stimulation of dopamine receptors is what leads to psychosis. There is also evidence showing that endorphins affect some dopaminergic neurons in the central nervous system. And that Naloxone changes some of the symptoms of schizophrenia (Borsook, 2017).

It also appears that the central limbic system of the brain represents the nerve center responsible for receiving the signal leading to poetry with activity or pleasure that leads to a state of addiction. When stimulating the medial limbic system, some neurons release dopamine, and this dopamine stimulates nerve cell membranes after the engagement, and then a nerve signal is generated that leads to a feeling of activity (Boecker et al., 2008; Bruehl et al., 2013) This condition leads the animal to search again for the substance leading to this feeling or feeling. It has been found that cocaine and the related addictive drugs inhibit the reabsorption of dopamine by the nerve endings, thus prolonging the duration of the dopamine effect, thereby increasing its stimulating effects with a sense of activity. Nicotine also affects the dopaminergic neurons themselves, except that it works by stimulating the release of dopamine and not by inhibiting its reabsorption, as is with cocaine. However, the final effects are the same as feeling energized and happy, and it is difficult to resist this habit (Hagelberg, 2012).

Conclusion

Endorphins are chemicals naturally produced by the nervous system to deal with pain or stress. They are released from the irritation of many nerve cells in the central nervous system. Endorphins are found in high concentrations in brain regions that contribute to the transmission of pain sensations, breathing, motor activity, secretion of pituitary hormones, and mood. And the relationship between endorphins and the stimulating hormone of the adrenal cortex came through behavioral studies that indicated that stress increases the concentrations of endorphins in the blood and brain. That's why they play an important role in relieving pain, decreasing

stress, and regulating hormones. It is also believed that endorphins may be important in regulating sexual behavior.

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Conflict of Interest

The author hereby declares no conflict of interest.

Consent for publication

The author declares that the work has consent for publication.

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