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Review Article

Endorphins-A Curative Medicine

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Abstract

Endorphins are endogenous opioids, neuropeptides, synthesize and stored in the pituitary gland. Beta-endorphin is an abundant endorphin, more potent than morphine, and binds with its μ receptors situated on the nervous system and immune cells. Which are involved in analgesic, anti-inflammatory, stress buster, and immune stimulatory activity. Because of these mechanisms of action, beta-endorphin can be used in the holistic management of cancer, autoimmune disease, psychological disease, neurodegenerative diseases, metabolic diseases, headaches, muscle spasms, and hormonal imbalances without adverse effects and is inexpensive. This article explains about beta-endorphin mechanisms of actions in chronic psychological stress-induced activation of HPA-axis-mediated various diseases.

Keywords: *HPA-Axis; NF-kB; STAT-3; ANS; IL-1; IL-6; TNF-α; IL-17; Tregs; TGF-β*

Introduction

Endorphins are endogenous opioids; neuropeptides; endomorphin's, synthesized and stored in the pituitary gland in response to physical stress and pain. Endorphins are more potent than morphine. There are three types of endorphins beta-endorphins, enkephalins, and dynorphins binds with μ, k, and Ơ receptors situated on the nervous system and immune cells [1-3,42]. Beta-endorphin is an abundant endorphin produced in the anterior pituitary gland. It is a precursor of POMC (Proopiomelanocortin), a large protein in response to CRH release from the hypothalamus at the time of psychological stress, cleaved to form beta-endorphin, MSH, and ACTH. Endorphin receptors are increased during stress full conditions such as inflammation haphazardly bind with endorphin receptors [4-6,43].

At the time of stressful conditions such as inflammation; the recruitment of immune cells to the site of inflammation produces endorphins. Endorphins inhibit pain and inflammation by inhibiting substance P, a neurotransmitter of pain and inflammation. Endorphins are produced during intense physical exercise and are known as Runner's high, sex, massage, meditation, yoga, acupuncture, chocolate consumption, and music therapy [7-9,44].

Beta-endorphin mechanism of actions

Beta-endorphins bind with its μ receptors situated on the PNS, resulting in the release of substance P, a neurotransmitter of pain and inflammation. Beta-endorphin binds with its μ receptors situated on the CNS, resulting in the inhibition of GABA inhibitory neurotransmitter and release of dopamine, an excitatory neurotransmitter involved in analgesic activity, stress buster activity, addiction, self-reward, euphoria, cognitive ability [10-12,45].

Beta-endorphins bind with its μ receptors situated on the innate and adaptive immune cells such as neutrophils, macrophages, NK cells, B cells, T cells, DCs, and mast cells results in activation of immune cells and inhibiting inflammatory mediators such as cytokines (IL-1, TNF-α, IL-6) and activating anti-inflammatory cytokines such as (Il-2, IL-12, IL-10 and IFN-δ), opsonin, granzyme B, IFN-δ and antibodies involved in anti-inflammatory activity, anti-tumor activity, antiviral activity, and immune stimulatory activity [13-15,46].

Applications of betaendorphin in human diseases

Beta-endorphins inhibits chronic psychological stress induced HPA-axis activation through ANS mediated release of stress releasing hormones such as cortisol, noradrenaline, ACTH, which will activate NF-KB, a key transcription factor, which in turn will activate through inflammatory mediators such as IL-1, TNF-α, IL-6 involved in tumor initiation, tumor promotion, and tumor progression by cell proliferation (Cyclin D, E), cell survival, BCL-2, BCL-XL), angiogenesis (IL-8, VEGF, COX-2), genomic instability (ROS, RNS, arginase1, AID), immune modulation (IL-4, IL-5, IL-10, IL-13, TGF-β), invasion and metastasis (UPA, Mmp's2, 9). It also involved in antagonize the activity of P53, a tumor suppressor, guardian of genome mutated in more than 50 percent of all cancers by ROS, RNS, and Arginase1 [16-18,47].

Beta-endorphin inhibits chronic psychological stress induced CRH (Corticotropin releasing hormone) release from hypothalamus-mediated HPA-axis activation through sympathetic nervous system of ANS release stress-releasing hormones such as cortisol, noradrenalin, ACTH, adrenalin, which activates inflammatory mediators such as IL-1, TNF-α, IL-6, in turn activates NF-KB, a key transcription factor, dysregulated NF-KB transcription factor involved in TH1 to TH2 lymphocytic conversion type release IL-4, IL-5, IL-10, IL-13, IL-17, TGF-β involved in cell injury, cell damage, chronic inflammation, immunomodulation and cell death [48, 49]. Growth factors such as EGF, FGF, VEGF activate NF-KB and STAT-3 transcription factor involved in cell proliferation, cell survival and angiogenesis. Altered regulated T cells (ATregs) formed from TH1 cells mediated by TGF-β release IL-10 and TGF-β involved in immunomodulation, otherwise n Tregs (Normal regulatory T cells) involved in self-tolerance and immune homeostasis [19-21].

Proteolytic enzymes such as UPa (Urokinase plasminogen activator) and Mmp's2, 9 are involved in extracellular matrix degradation-induced cell damage and tissue injury. All these changes lead to autoimmune disease [22,23].

Beta-endorphin delays aging by lengthening telomeres, which otherwise shortens with aging by oxidative stress and NF-KB, a key transcription factor induced release of ROS, RNS free radicals activated by psychological stress-induced CRH (corticotrophin-releasing hormone) release from hypothalamus activates the release of stress releasing hormones such as cortisol, ACTH, adrenaline, noradrenaline through HPA-axis mediated sympathetic nervous system of ANS activates inflammatory mediators such as IL-1, TNF-α, IL-6 involved in activation of NF-KB transcription factor release ROS, RNS free radicals involved in cell injury, cell aging, and cell death [24-26].

Beta-endorphin inhibit chronic psychological stress-induced CRH from the hypothalamus activates the HPA-AXIS mediated sympathetic nervous system of ANS releasing cortisol, adrenalin, and noradrenalin stress-releasing hormones involved in the release of glucose from the liver to blood known as gluconeogenesis leads to an increase in blood sugar level known as diabetes and also involved in release of hormones such as TSH by activation of ACTH leads to hypothyroidism and stress releasing hormones such as cortisol, adrenalin, and noradrenalin at higher levels involved in activation of inflammatory mediators induced immunomodulation leads to tissue damage known as thyrotoxicosis [27-29].

Beta-endorphin inhibits chronic psychological stress-induced release of CRH from hypothalamus and activates HPA-axis through the sympathetic nervous system of ANS release stress releasing hormones such as cortisol, noradrenaline, and adrenaline involved in constriction of blood vessels in the brain and muscle spasm leads to headache [30-33].

Beta-endorphins inhibits chronic psychological stress induced CRH (Corticotropin releasing hormone) mediated by HPA-axis through sympathetic nervous system of ANS releasing factors such as cortisol, ACTH, adrenaline, and noradrenalin activate inflammatory

mediators such as IL-1, TNF-α, and IL-6 from chronic inflammatory cells such as macrophages, neutrophils, and mast cells, which in turn activate NF-KB, a key transcription factor constitutive activation involved in transcription of inflammatory mediators results in chronic inflammation by IL-4, IL-5, IL-13, IL-17 involved in cell injury, tissue damage, cell death. Injury to tunica intima of coronary blood vessels leads to plaque formation, ischemia, and heart diseases (Angina pectoris and Myocardial infarction) [34-38].

Beta-endorphin inhibits chronic psychological stress induced CRH (Corticotropin releasing hormone) from hypothalamus mediated by HPA-axis through sympathetic nervous system of ANS (Autonomic nervous system) and activating parasympathetic nervous system releasing stress-releasing hormones such as cortisol, ACTH, adrenaline, and noradrenaline activate inflammatory mediators such as IL-1, TNF-α, and IL-6 from inflammatory cells such as macrophages, neutrophils, and mast cells, which in turn activate NF-KB, a key transcription factor constitutive dysregulated activation results in activation of chronic inflammatory mediators involved in the formation of plaque(amyloid deposition) in the brain leads to cognitive decline and dementia later leads to Alzheimer's disease [35,39-41].

Conclusion and Future Perspective

Endorphins are natural opioids, produced in the pituitary gland in response to physical stress and pain. Beta-endorphin, an abundant endorphin can be used in metabolic disease, neurodegenerative disease, psychological disease, cancer, and autoimmune disease by binding its μ receptors on the central and peripheral nervous system, immune cells involved in analgesic, anti-inflammatory, stress reduction, and immune stimulatory activity. A thorough understanding of beta-endorphin synthesis, and its receptors, production, mechanisms of action, dose-dependent duration of action, and applications in various diseases, helps in the safe and effective holistic management of various diseases without adverse effects and is inexpensive.

Conflict of Interest

None.

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