

'Happiness' - The Role of Neurochemicals

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Abstract: *Happiness, the feeling that occurs when you are aware that life is good, and you smile for that sole reason. Happiness is a sense of joy, well-being, pleasure, satisfaction or contentment. Happiness is influenced by several factors both exogenously and endogenously. Amongst all the endogenous determinants, the role of neurochemicals tends to be the most dependent predictor of happiness. The aim of the study was to gather this information about the neurochemicals that predominantly affects happiness directly or indirectly. Several hormones, neurotransmitters and other endogenous compounds were under search to gain a significant conclusion. For this, all the already known and those yet to be known neurochemicals that influenced happiness some or the other way were searched for in the google search engine and data were obtained from certain websites like PubMed, Psychology today, Encyclopedia etc. and later these data were organized in a systematic manner to obtain 12 different neurochemicals that are influencers of happiness. The basic structures of these organic compounds were also gathered to present the idea clearly. Out of all the 12 neurochemicals, serotonin, dopamine, oxytocin and endorphins were purely independent and accurate predictors of happiness and had significant role in its biochemical aspects. The remaining were found to affect happiness either indirectly or by directly stimulating the higher centers of the brain. From this, it can be concluded that the major endogenous factors that exaggerate the feeling of happiness or bring about itself are the release and actions of such neurochemicals.*

Keywords: Neurochemicals, Happiness, Hormones, oxytocin, dopamine, endorphin, serotonin, endocannabinoids

1. Introduction

Neurochemicals are certain organic peptides or substances secreted from different endocrine and paracrine cells, nerve endings and some other tissues of the body that participate in the activities or functions of the brain. Emotions are conditions of the mind produced in response to internal or external stimuli that are duly influenced by these neurochemical releases. Happiness is the most preferred emotion of mankind and is a state of feeling good at heart or can express it through smile or laughter. It is highly correlated with peace of mind and affects the mood of an individual. Happiness is an emotion produced as a response to an individual's feeling of well-being in all aspects and it has a wide array of factors governing its fullness. All these factors are a function of different neurochemicals secreted from several parts of the body and are under discussion in detail.

Oxytocin

Oxytocin is an oligo-peptide hormone with 9 amino acids and is released from the neurohypophysis. It is synthesized mainly in the paraventricular nucleus and partly in the supra-optic nucleus of hypothalamus and is released into the posterior pituitary via the hypothalamo-hypophyseal tract. It is released in response to 2 stimuli, suckling during breast feeding, and dilatation of the cervix during parturition.¹ It is thus an important hormone in the regulation of uterine spasms and milk ejection.

Role in Happiness

Oxytocin is referred to as the 'bonding molecule' or 'hug hormone' because its levels go high during feeding the baby, skin-skin contact, intercourse, orgasm, and hugging. It's also a hormone involved in increasing the trust and loyalty as per recent studies and is known to cause romantic

attachment². In other words, it is known to facilitate social interaction and is also linked with positive social behavior. Such a significant correlation between social bonding and satisfaction, then indeed brought about by the effects of oxytocin can in turn lead to a happier life. It has been recently showed that, Oxytocin causes a huge scale of physiological and behavioral effects controlled via certain receptors in the brain, mainly, social, sexual and maternal behaviours³. Being associated with positive social behaviors and known to increase the relationship or bonding with others, it's assumed that the hormone brings about happiness. Because relationships have a strong impact on life satisfaction and as there is a strong association between happiness and relationships, oxytocin can be a method of producing happiness by stimulating or strengthening social relations.^{4, 5} Low levels of oxytocin is associated with depression, poor communication, increased fear and anxiety, sleep disturbances, irritability and cravings for sugar.⁶ Gifting can increase the release of the hormone established by increasing the bonding between the receiver and giver.⁷

Endorphins

Endorphins or endogenous morphine are opioid neuropeptides which are naturally produced in the body. Endorphins function not only as neurotransmitters but also as peptide hormone. It is known to be derived from repeated cleavage of its precursor molecule, pro-opiomelanocortin (POMC) polypeptide, synthesized in the pituitary gland and in some amounts by the immune system of the body.⁸ There are 3 functional sub-types based on the process of cleavage named alpha-endorphins, beta-endorphins and gamma-endorphins. They are known to be an endogenous analgesic that blocks the perception of pain, involved in pleasure sensations.

They form a major part of the endogenous pain inhibiting systems of the body.

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Role in Happiness

Endorphins or 'pain-killing molecules' or 'pain relievers' have been found to be 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 is one of the 4 major hormones of happiness or pleasure hormones.⁶ It's believed that the feelings of pleasure persists to make us realize at 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.^{6,7} Clinically, endorphins have been associated with conditions of autism, depression, and depersonalization disorder and physiologically known to be related with activities like laughter and vigorous aerobic exercise.^{9, 10, 11}

Serotonin

Also known as 5-hydroxytryptamine (5-HT), serotonin is a complex neurotransmitter. It is distributed in various body tissues like CNS, GI tract etc. and known as enteramine due to its increased concentration in the intestine. It is a derivative of the branched-chain amino acid, tryptophan and is metabolized to 5-Hydroxyl Indole Acetic Acid (5-HIAA).³ It performs several functions in the body that is, causes generalized vasoconstriction, bronchoconstriction, increases gastric secretions and motility, causes platelet aggregation, is anti-diuretic in nature, important component of the endogenous analgesic system, acts as anorectic agent, suppresses sleep and is a strong anti-depressant.

Role in Happiness

Serotonin is known as the 'confidence molecule' as it brings about confidence and self-esteem and there is a positive feed-back loop that causes further release of the chemical through building up self-esteem.² It controls an immense spectrum of physiological and biological actions like arousal, aggression, mood, memory and abilities of thinking.⁶ Raised levels of serotonin are identified during states of self-confidence, feeling of a self-significance and causes relaxation from which it's clear that absence of serotonin imparts feeling of being depressed or lonely.⁷ They belong to a wide range of anti-depressants called Serotonin Specific Reuptake Inhibitors (SSRIs) indicating their role in mood up-liftment.^{6,7} Excess levels of serotonin induces sedation and apathy, while lower levels of serotonin is attributed to less mood, depression, poor control of appetite, anxiety disorders, lack of will, social and sexual behavioral problems.

Dopamine

Dopamine (DA) is a catecholamine neurotransmitter, biogenic amine and an adreno-medullary hormone. It is the principal neurotransmitter of several pathways in the Central Nervous System (CNS) starting in the midbrain and significantly involved in motivation, learning, and motor activity, any disturbances of which have been associated with several disorders, including Parkinson's disease and schizophrenia.¹² Dopamine is catecholamine secreted from the medulla of adrenal glands. It belongs to the phenethylamine family and functions as both a hormone and

neurotransmitter in several parts of the body. Normal plasma dopamine levels are very low, i.e., 0.13nmol/L.¹³ Its effect as a catecholamine includes renal and mesenteric vasodilatation, vasoconstriction of other parts of the body. Dopamine has positive inotropic effects on the heart mediated via β_1 receptors. It causes an increase in systolic Blood Pressure and do not affect Diastolic Blood Pressure significantly. In the proximal tubules, it inhibits the sodium-potassium pump and causes natriuresis. Also, highly intervened for the treatment of traumatic and cardiogenic shock.³

Role in Happiness

Dopamine is known to be a 'reward molecule' and is normally thought to be involved with anticipation.^{2, 14} In the brain, it feeds the reward pathways, and is concerned with addiction, drive, motivation and pleasure, ovulation and muscle control. It is also known to be associated with vigilance, alertness, cognition, memory and happiness. High levels of dopamine are associated with, loss of consciousness with reality, lack of emotion, additive behavior, suspicious personality, possible paranoia and delusions, while significantly low levels are linked to depression, mood swings, attention deficit, cognitive issues, compulsive behavior, cravings, apathy, loss of satisfaction in life activities risk taking and additive behavior.^{6,15} Dopamine is known to be a reward molecule as it is continuously found to be released on achievements like scoring a goal, hitting a target or accomplishing a task in reward from the brain telling that he/she has done a good job. Also, dopamine is known to be released naturally on showing kindness to others and even thoughts of loving kindness can elevate dopamine levels. Volunteering has also been known to cause release of dopamine.¹⁶

Estrogens

Estrogens are certain ovarian steroid hormones secreted from the granulosa cells of follicles of ovary, corpus luteum and placenta. It is also indirectly released from adrenal glands as the androgens are converted to estrogen by the enzyme aromatase. The naturally synthesized estrogens include 17 β -estradiol, estrone and estriol, the former being 15 and 80 times potent than the respective latter ones. It is mainly synthesized from cholesterol and its mechanism of action is through transcription of mRNAs. The major action of estrogens includes, promotion of growth of all components of female reproductive system including ovary and ovarian follicles, stimulation of smooth muscle contraction in fallopian tube, increases uterine size, its blood flow, causes proliferation of uterine endometrium etc. Under the presence of estrogen, cervical mucous becomes abundant, watery and clear and male female secondary sexual characters develop. Estrogen stimulates libido by acting on the limbic system neurons and can also help in bone growth. On kidneys it regulates salt and water retention and activates Renin-Angiotensin-Aldosterone system. Estrogen also acts as a cholesterol lowering agent, promotes more fluid secretion from sebaceous gland and thus prevents acne.³

Role in Happiness

Estrogen is known to be a happy hormone due to its indirect effect in stimulating the formation of serotonin. This can

protect the body from conditions of irritability and anxiety, thereby keeping the mood constant.¹⁷ It is also known to cause increased secretion of endorphins both of which are chemical messengers linked with positive states of mood. Estrogens can cause mood disruptions in women, failure of synthesis or low levels of which can result in mood swings, anxiety and depression. High levels of estrogen can also be dangerous. Estrogen has also a role in regulating the levels of hormones like serotonin, endorphins and nor-epinephrine by causing a decline in the level of the enzyme mono-oxidase that deactivates these hormones hence referred to as 'positive mood hormone'.⁶

Progesterone

Progesterone is a C-21 steroid hormone secreted by corpus luteum and placenta during pregnancy period. A small amount is also released from adrenal cortex and testes. The normal plasma levels of the hormone vary with different phases of the female cycle, although it reaches its peak in the luteal phase, that is, 18ng/ml. Progesterone has both reproductive and non-reproductive actions on the body. Reproductive actions are primarily focused on the reproductive organs mainly uterus, endocervix, vagina, fallopian tubes and breasts. Other systemic actions are on kidney, CNS, Respiratory system, fat metabolism and thermo-genic effects.¹⁸

Role in Happiness

Progesterone alters the secretion of several neurotransmitters in the brain affecting appetite and sleep.¹⁸ It causes the effect of somnolence, that is helps to sleep well and thereby prevents anxiety, feelings of irritability and mood swings.¹⁷ This can help in maintenance of a peaceful or calm state of mind. Progesterone due to its Valium-like effect of its metabolite named allopregnanolone (ALLO), is known to soothe the mood. ALLO interacts directly with the receptors of GABA promotes sleep. Progesterone also has a control on the DAO enzyme and therefore relieves the symptoms of anxiety in the condition of histamine intolerance.¹⁹ Progesterone also seems to activate the activity of amygdala, the chief alert system of the brain.²⁰

Endo- Cannabinoids

Endocannabinoids (ECs) are defined as the endogenous ligands of cannabinoid receptors (CB1 and CB2) and a growing body of evidence has emerged on the role of the endocannabinoid system (ECS) in the regulation of several physiological conditions and numerous conditions.²¹ These are certain lipid metabolites and has both juxtacrine and paracrine roles in intercellular communications.²² These are self-produced cannabinoids and works on the CB-1 and CB-2 receptors of the cannabinoid system and Anandamide is the most known among them.² The endocannabinoid system is another protective system of the body that regulates many physiological functions. This includes endocannabinoids, cannabinoid receptors, and enzymes that synthesize and degrade endocannabinoids.²³

Role in Happiness

Cannabis compounds are actually called as "bliss molecules" that enhances the subjective concept of well-being by activating the endocannabinoid system (ECS), and modulates almost all of the response to stress, reward, and

also the interactions between them.^{2, 24} There are much evidences that endocannabinoids control mood, emotion, memory, motivation, perception of pleasure, metabolism, and appetite and so on. The association between cannabinoids and different states of emotion has empirically and scientifically been established for long. The first active ingredient of the system was discovered from the cannabis plant (*Cannabis sativa*) and is delta9-tetrahydrocannabinol (delta9-THC), and even it tends to produce euphoria and enhancement of sensory perceptions.²⁵ The discovery of endocannabinoids opened a new pathway to the biochemistry of happiness for previously it was named after serotonin and dopamine. The name of the well-known endocannabinoid, anandamide itself (ananda - Sanskrit word meaning "joy, bliss or happiness") reveals its role in mood states. Recent researches also show a strong association between the serotonergic and endocannabinoid systems.²⁶ The connection between depression, anxiety, mood disorders, emotional states and cannabinoids is an established fact, and a lot of research is currently focusing on it. The genes that code for these receptors also determine their role in bliss for CB-1 genes exhibit polymorphisms bringing about a variety of differences. Also, an individual with a specific genetic code for CB-1 receptor tend to be much happier and responds better to positive stimuli. They are also known to play an important role in response to stress, that is, they are compounds released in response to diverse stimuli of stress and thereby protect the body and helps in stress management.

Adrenaline and Nor Adrenaline

Adrenaline (epinephrine) is a primary catecholamine synthesized from the adrenal medulla and constitutes about 85% of the total catechol amines, however, smaller amounts are synthesized in the brain.¹⁸ Nor-adrenaline (Nor-Epinephrine) accounts for about 10-15% of the adreno-medullary secretion and after synthesis both of them are stored in the granules of chromaffin cells of the gland before their secretion.³ The normal plasma concentration of epinephrine is 30pg/ml and that of nor-epinephrine is 300pg/ml. These are short spanned hormones and are conjugated to sulfate in the liver and kidney after its utilization. Epinephrine is known to increase Heart Rate and force of myocardial contraction causing increase in Cardiac Output and subsequent increase in Systolic Blood Pressure. Acts as a major vasoconstrictor in the splanchnic, cutaneous and renal vascular bed and as a vasodilator in the skeletal and hepatic circulation. Being secreted during states of stress, it's known to be primarily responsible in the fight or flight response of the body.³ Nor-epinephrine causes vasoconstriction mediated via alpha-1 receptors in most organs of the body, increasing peripheral resistance and thereby diastolic blood pressure. On heart, it is positively inotropic and chronotropic thereby increasing systolic blood pressure. The net effects of the hormone are decreased heart rate and cardiac output or simply antagonistic to the action of epinephrine due to baroreceptor reflex activity.³

Role in Happiness

Adrenaline is termed to be the "energy molecule" as its release causes an energy surge. This surge helps us feel lively and can be an antidote for malaise, stagnation and boredom.² Urinary adrenaline is known to be a good

predictor of happiness, which was derived from the fact that individuals with higher 'personal growth' and 'purpose in life' had a lower level of urinary adrenaline.²⁷ 'Adrenaline rush' helps an individual undergoing distress to feel very much alive and provide he/she with the energy to cope up with that situation.¹⁶ Nor- adrenaline is a stress hormone which control and co-ordinates the fight-or-flight response along with the chemically similar counterpart, adrenaline. It regulates much of the physical parts of emotion, mainly, raised heart rate and also acts on certain brain centers stimulating alertness, cognition and decision-making behavior.¹⁵ Low levels of nor- epinephrine have been associated to depression, and further studies suggested that certain norepinephrine "re-uptake inhibitor antidepressants that are highly selective "influences a positive emotional and perceptual bias in healthy individuals."²⁸

Gamma Amino Butyric Acid (GABA)

GABA is an inhibitory neurotransmitter in the Central Nervous System (CNS). It is synthesized by the decarboxylation of glutamate.¹⁸ It is termed to be inhibitory as it inhibits or blocks certain signals in the brain decreasing the brain activity.²⁹ The receptors of GABA causes pre-synaptic inhibition (indirect).¹⁸ The medical conditions in which low levels of GABA are found include: seizures, anxiety, attention deficit hyperactivity disorder, movement disorders, mood disorders etc.²⁹

Role in Happiness

Activation of GABA improves mood indirectly and makes it possible by easing stress and anxiety.³⁰ In case of feeling down but not being anxious or stressed, GABA may not exert its effect on happiness or being calm but in case of feeling stress and blue or anxiety, GABA may help lift the mood and bring a little more relaxed happiness.³¹ GABA plays an important role in regulation of many physiological and psychological processes by inhibition of neuron signaling in the brain. So, dysfunction of this system is indicated in the pathophysiology of anxiety and depression.³² For this reason, GABA is known as the 'anti-anxiety' molecule and creates a sense of calmness.²

Cortisol

Cortisol is known to be the life- saving hormone and is secreted from the zona fasciculate layer of the adrenal cortex regulated by the Corticotrophin releasing hormone (CRH) Adrenocorticotrophic Hormone (ACTH). It's a steroid hormone synthesized from cholesterol and is transported through plasma in free as well as bound forms (transcortin is the cortisol binding protein). Being a steroid hormone, its mechanism of action is via the gene- regulatory elements of the cell, the receptors are glucocorticoid receptors. Normal plasma levels of cortisol are 14µg/dl and it acts almost all systems of the body. Major functions are involved in metabolism, stress, myocardial performance and vascular reactivity, mood and behavior, bone formation and resorption, maturation of CNS, hemopoiesis, immunity, and gastric secretions and on other endocrine hormones.³

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The primary and most important function of cortisol is to save the body in stressful conditions. Stress is in fact

described as the condition in which there is an increased secretion of ACTH.³ The role of cortisol is in managing stress and as per indicated by different studies, the relationship between cortisol and depression is a reverse dimension of happiness.³³ Also, Cortisol is a congruous marker for depression. Raised levels of early morning Cortisol have been associated to depression and neuroticism.³³ Atypical secretion patterns of the hormone have been related to stress, anxiety and depression.³⁴ Researchers, based on these findings, concluded that happiness is indirectly linked to the cortisol levels in the body.

Melatonin

Melatonin or N- acetyl-5-methoxytryptamine is a peptide hormone secreted from parenchymal cells of the pineal gland and is synthesized from tryptamine. The secretions at peak during the night time. There are 2 types of receptors for the hormone: ML1 and ML2. The secretion has a definite diurnal pattern those co-ordinates the different endocrinal responses of the body with changes in light and dark environments. It is known as the 'biological clock' and maintains the diurnal rhythm or sleep- wake cycle. It's also known to cause inhibition of gonadal functioning and thereby onset of puberty.

Role in Happiness

The hormone is associated with the mechanism by which our body becomes ready for sleep.³³ Studies already conducted provides proof for the assumption that melatonin level is linked to the level of happiness. Melatonin is known to have a role in depression and few of the antidepressants raises the melatonin levels in blood.³⁵

2. Recommendations

Further studies are required to precisely evaluate the biochemical roles of these neurochemicals in the physiology of happiness.

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