Iranian J Publ Health, Vol. 43, No.11, Nov 2014, pp. 1468-1477

Review Article

Happiness & Health: The Biological Factors- Systematic Review Article

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(Received 23 July 2014; accepted 12 Oct 2014)

Abstract

Happiness underlying factors are considerable from two dimensions: endogenic factors (biological, cognitive, personality and ethical sub-factors) and exogenic factors (behavioral, social-cultural, economical, geographical, life events and aesthetics sub-factors). Among all endogenic factors, biological sub-factors are the significant predictors of happiness. Existence of significant differences in temperament and happiness of infants is an indicator of biological influences. Therefore, this study aimed to consider biological factors that underlie happiness. At the first, all of the biological factors in relation with happiness were searched from following websites: PubMed, Wiley& Sons, Science direct (1990-2014). Then, the articles divided into five sub-groups (genetic, brain and neurotransmitters, endocrinology and hormones, physical health, morphology and physical attractiveness). Finally, a systematic review performed based on existing information. Results of studies on genetic factors indicated an average effectiveness of genetic about 35 -50 percent on happiness. In spite of difficulties in finding special genes, several genes distributed to emotion and mood. Neuroscience studies showed that some part of brain (e.g. amygdala, hipocamp and limbic system) and neurotransmitters (e.g. dopamine, serotonin, norepinefrine and endorphin) play a role in control of happiness. A few studies pointed to the role of cortisol and adrenaline (adrenal gland) and oxitocin (pituitary gland) in controlling happiness. Physical health and typology also concluded in most related studies to have a significant role in happiness. Therefore, according to previous research, it can be said that biological and health factors are critical in underlying happiness and its role in happiness is undeniable.

Keywords: Happiness, Health, Biological factors

Introduction

During the history of psychology, this branch of science studied the human being disorders such as anxiety, depression, and violence and so on. First, the goal of clinical professions was treating patients' states from negative to normal, or as Seligman suggested "from minus five to a zero"(1). This perspective in psychology called negative psychology. After World War II, positive psychology developed as a new area. Positive psychology emphasized that psychology is not only studying impairments, injuries and disorders, but it can study the strengths and abilities of individuals. Positive psychology included such contents as Happiness, Life quality, Optimism and so on (2).

For decades, researchers tried to study and understand happiness predictors. Some researchers be-

lieve that happiness is due to genetic and inherited factors and others believe that happiness caused by environmental factors like: high income, education, being active during life. Results of previous studies suggest that happiness is not caused by just one or two factors but it is a result of integrated several factors. As a whole, two general factors influence emotions in individuals. Happiness as an emotion formed as a general interaction between internal (endogenic) and external (exogenic) factors. It must be noted that each factor has a different weight in this relation (2-4).

Biological factors as endogenic factor are significant predictors of happiness. Of course, happiness is not a typical subject that investigated by biologists, but a biological perspective is useful for interpretation of happiness or the quality of life (2). Therefore, this study aimed to consider biological factors that underlie happiness.

Methods

At the first, all of the biological factors in relation with happiness were searched from following websites: PubMed, Wiley& Sons, Science direct (1990-2014). Then, the articles divided into five sub-groups (genetic, brain and neurotransmitters, endocrinology and hormones, physical health, morphology and physical attractiveness). Finally, a systematic review performed based on existing information.

Genetics Factors

In the recent years appeared a new branch of human psychobiology: a genetic approach to well-being and happiness. Twin studies suggested that genetic factors count for 35 -50 percent of happiness (5).

In a comprehensive investigation, happiness (subjective well-being) was measured in a birth-record-based sample of several thousand middle-aged twins using the Well-Being scale of Multidimensional Personality Questionnaire. Socioeconomic status, educational attainment, family income, marital status, an indicant of religious commitment could not account for more than about 3% of the variance in well-being. However, from 44% to 52% of the variance in well-being were associated with genetic variation. When twins have been retested after few years, authors found that the heritability of the stable component of subjective well-being approaches 80% (6).

What kind of genetic mechanisms make a person happy? It is an important question in this field. Finding special genes in happiness is a difficult task, but recently progresses in molecule genetic open a new way to neurobiology markers of happiness. Therefore, we hope to find the answer and now several genes for mood and emotional characteristics identified (Table 1). Most of studies focused on mood disorders such as depression (7). More specific studies about happiness needed to clarify our knowledge.

Among all related genes with mood and emotional characteristics, effects of two genes investigated directly on happiness: *5-HTTLPR*and *MAO-A*

Studies suggested an association between *5-HTTLPR*and life satisfaction as a cognitive dimension of happiness (8-11). This gene is coding serotonin distribution in brain cells and therefore leads to mood regulation. There are two different functional forms for this gene: Long one (L), Short one (S). L produces transporter- protein molecules and conducts serotonin transmitter in nerve cells. S produces high-level activity for the serotonin – dependent brain system that regulates mood and behavior. Each person has two kind of a gene that called allele and each of them inherited from parents. However, some people have two S alleles and another people have one L and one S. people who have one L, their life satisfaction is 8% more than others are. Those who have two L allele, their life satisfaction are 17% more than people that have just one S allele. In subjects with L version 35% are very satisfied with life, 34% are satisfied while in subjects with S version only 19% are satisfied(9). *MAO-A* is introduced as a gene that involved in regulating happiness. This gene that located on chromosome X involved in mood regulation and it is a catabolic enzyme for serotonin, dopamine, and noradrenalin (12, 13).

Table 1: Genes related to mood and emotional characteristics (8)

Genes	Associations
DRD2	Alcoholism, Substance abuse, craving behavior, cocaine dependence, smoking, ADHD, parenting, Obesity, video gaming, sexual activity, posttraumatic stress disorder schizophrenia, Parkinson's, brain metabolism, BMI, executive functioning, love styles (EROS) pathological gambling. Pathological aggression, schizoid/avoidant behavior, criminal activity, politics party attachment. Energy, hypertension.Hyperphagia, growth, sexual maturation, brain development, depression, anorexia, bulimia, fibromyalgia, pain sensitivity, hunger, novelty seeking, extraversion, early onset sexual intercourse, defense style (lying), oppositional defiant disorder, panic disorder, developmental personality, Tourette Syndrome, Parkinson's, executive dysfunctioning, pleasure "buzz
ANNKI	Smoking dependence, parental rule-setting, Schizophrenia, cognition deficit, alcohol and opiate dependence, pleasurable "buzz",
5HT2A	Eating disorders, obesity, Insulin resistance, love styles (romantic), suicide, ADHD, Panic disorders, impulsive aggression, cognitive impulsivity, anger, sweet tooth, antidepressant treatment outcomes, fibromyalgia, obsessive-compulsive disorder, borderline personality, smoking behavior, cocaine dependence, BMI.
OPRK1 (kappa-opioid receptor)	Alcohol and heroin dependence. Pain mechanisms and tolerance.
OPRM1 (mu-opioid receptor)	Pleasure "buzz", smoking addiction, heroin addiction, alcoholism, pain sensitivity, BMI, type 2 diabetes mellitus.
COMT	Psychiatric and affective disorders, alcoholism, substance use disorder, smoking, post-surgical pain, fibromyalgia, Parkinson's disease, ADHD.
SLC6A3	Post-surgical pain, cocaine abuse, alcohol dependence, smoking behavior, juvenile delinquency, pathological aggression, bipolar disorder, schizophrenia, ADHD, impulsive aggression, cognitive impulsivity.
HTR3B	Heroin addiction, migraine, impulsive behavioral aggression, cognitive –impulsivity, ADHD alcoholism.
NOS3	Pain mechanism, healing mechanisms, circulation, hypertension, cardiovascular.
PPARG	Type 2 diabetes, Obesity, Insulin sensitivity, Body composition, eating disorders, BMI, physical exercise, common metabolic disorders, body mass, waist circumference, inflammatory response, immune system.
CHREBP	Plasma triglycerides, triglyceridemia, obesity „improves plasma glucose,
FTO	Severe obesity, food intake, adiposity, body mass, energy intake, BMI, fat mass, pleasurable "buzz".
TNF alpha	Inflammation, mortality, schizophrenia, bipolar disorder, BMI, Immune response.
PEMT	Proinflamamtory, immuneregulation, apotosis, substance use disorder.
MANEA	Substance dependence
LEPTIN-OB	BMI, Schizophrenia, stress, obesity risk, food intake, craving behavior, diabetes, insulin sensitivity, adiposity, body composition, linear growth, metabolic factors, hyperphagia, cocaine dependence, lip genesis, modulation of sweet substances, anorexia, bulimia, cardiovascular effects, fertility, sexual maturation, brain development, depression, fatty acid metabolism, hunger,
MAO-A	Pain sensitivity, bipolar affective disorder, ADHD, alcoholism, Substance Use Disorder, violent behavior, juvenile delinquency, smoking, child abuse, suicide, criminal activity, posttraumatic stress disorder, antidepressant treatment response, alcoholism, panic disorder, schizophrenia, pathological gambling.
ADIPOQ	Metabolic syndrome, adiposity, fat mass, energy intake, obesity, lipogenesis, type 2 diabetes, BMI.
STS	ADHD
VDR	Obesity, BMI, overeating, metabolic syndrome, anthropometric measures, schizophrenia, temporal lobe epilepsy, immune system, type 2 diabetes, physical activity, BoneDensity (Osteoporosis).
DBI	Anxiety Disorders
GABRA6	Autism, alcoholism, stress response.
GABRB3	Autism, alcoholism, stress.
MTHFR	Cardiovascular disease, Homocysteine levels, obesity, fat mass, Schizophrenia.
MLXIPL (CARBOHYDRATE BINDING ELEMENT)	Plasma triglycerides, glucose craving behavior, obesity.
VEGF	Angiogenesis factor, cognition, tissue healing, pain sensitivity, oxidative stress.
DRD4	Financial risk taking, nicotine withdrawal, ADHD, novelty seeking, Alcoholism, aggression, impulsivity, delinquency, memory deficits, anger, temperament, schizophrenia, sexual intercourse, drug abuse, extraversion, obesity, stress, emotional reactivity, infant attachment, oppositional defiant disorder, fibromyalgia, hyperphagia, alcohol craving, pathological gambling, panic disorder, developmental personality, Tourette Syndrome, Parkinson's.
VMAT2	Antidepressant treatment outcome, Parkinson's, ADHD, cocaine and methamphetamine dependence, spirituality"GOD Gene".
CLOCK	Circadian system, mood, bipolar, endocrine and metabolic rhythms, stress, reproduction, morphine dependence
MELATONIN	Sleep anxiety, alcoholism
OREXIN	Hyperphagis and energy regulation

"MAO-A, possesses a variable number of tandem repeats polymorphism (*MAO-A-uVNTR*), resulting in genotypes with low-activity (*MAO-A-L*) and high-activity (*MAO-A-H*) alleles" (13). The *MAO-A-L* allele is a risk factor for stress-related negative consequences such as alcoholism aggressiveness and antisocial problems (14-16).
Researches indicated that in women, the low expression allele of the monoamine oxidize (*MAO-A-L*) gene predicts higher self-reported happiness (13).

Brain and Neurotransmitters

All of the activities managed by brain. Thoughts, feelings, activities, learning and love, all conducted by brain. Mood and emotions are not except for this role.
"The emotion circuitry of the brain is complex, involving primarily structures in the prefrontal cortex, amygdale, hippocampus, anterior cingulated cortex, and insular cortex. These structures normally work together to process and generate emotional information and emotional behavior. Research has particularly focused on the prefrontal cortex which, unlike most other brain regions involved in emotion processing, shows asymmetric activation in relation to positive and negative emotions"(17).Davidson and his colleagues have reported large individual differences in baseline levels of asymmetric activation in prefrontal cortex, related to a person's typical emotional style. Individuals with a positive emotional style show higher levels of left than right prefrontal activation at rest (using EEG or fMRI), while those with a negative emotional style tend to show higher levels of right than left prefrontal activation at rest (18-20). Davidson and colleagues have also reported that, independent of emotional style; induced negative mood increases relative right-sided activation, whereas induced positive mood increases relative left-sided activation (21).
Limbic system that is placed in the central area of brain has the most influence on identifying the form of emotions. Increasing in metabolism of limbic system leads to depression in individuals.
At the other hand, studies showed that positive and negative moods affected by brain chemical in several ways. Two of the most important neurotransmitters that involved in mood are dopamine and serotonin. Positive mood and negative mood mediated by dopamine and serotonin levels.
Perhaps the most influential neurochemical theory of positive mood is presented by Ashby et al. (22). The two main elements of their theory are that: (i) positive mood is associated with (but not necessarily caused by) increased levels of dopamine in the brain and (ii) some of the changes in cognition observed in positive mood are due to the increased dopamine levels associated with positive mood.
In contrast, Ashby et al. argue that the effects of negative mood are against of positive mood. One might predict that negative mood is simply associated with lower dopamine levels (22).
Another neurochemical agent that associated with emotional states is serotonin (*5HT*). Serotonin is a neurotransmitter that mediated satisfaction, happiness and optimism. Serotonin levels are reduced in depression, and most modern anti-depressant drugs, known as serotonin reuptake inhibitors (*SSRIs*), act by increasing the amount of serotonin available to brain cells. However, what is the relationship between serotonin and positive mood? Researches indicated that increased of serotonin level was related to positive mood (23).
Norepinephrine is another neurotransmitter that associated with the level of happiness. Antidepressants such as the selective norepinephrine reuptake inhibitor (Reboxetine) also induce a positive emotional perceptual bias in healthy subjects suggesting that norepinephrine positively colors the emotional perception of facial expressions in humans. "Recognition that norepinephrine regulates neuronal excitability in the basolateral amygdale by facilitation of GABA release, demonstrates a potential neuroanatomical locus for this effect"(24).
Endorphin also studied as a neurotransmitter in happiness. Endorphins are endogenous opioid peptides that function as neurotransmitters. They are released during continuous exercise, fear, love, music, chocolates eating, laughter, sex, orgasm etc. Increased level of endorphin inhibited pain in the

body and reduced level of endorphin inhibited positive feelings.

"In most of the diseases doctors suggest exercises such as walking, running, workouts, laughing exercise, meditation, listening music and all these exercises are responsible for the release of endorphin hormone or they are the stimuli to release this hormone which gives them strength, confidence and gives a good mood to them a mood of well-being and happy"(25).

Melatonin or n- acetyl- 5- methoxytryptamine is a hormone that is made by the pineal gland in the brain during night. It is linked with how our body gets ready for sleep. Melatonin levels vary in 24-hour cycles and are controlled by being in bright light. Its level increase in general between 21 to 22 and then decrease in the morning (26). Studies showed that melatonin level is related to happiness level. Melatonin has a role in depression and some of antidepressants increase the melatonin in blood (26).

Since each neurotransmitter coded by a special gene, genetic factors have a clear and significant effect on happiness (Fig.1).

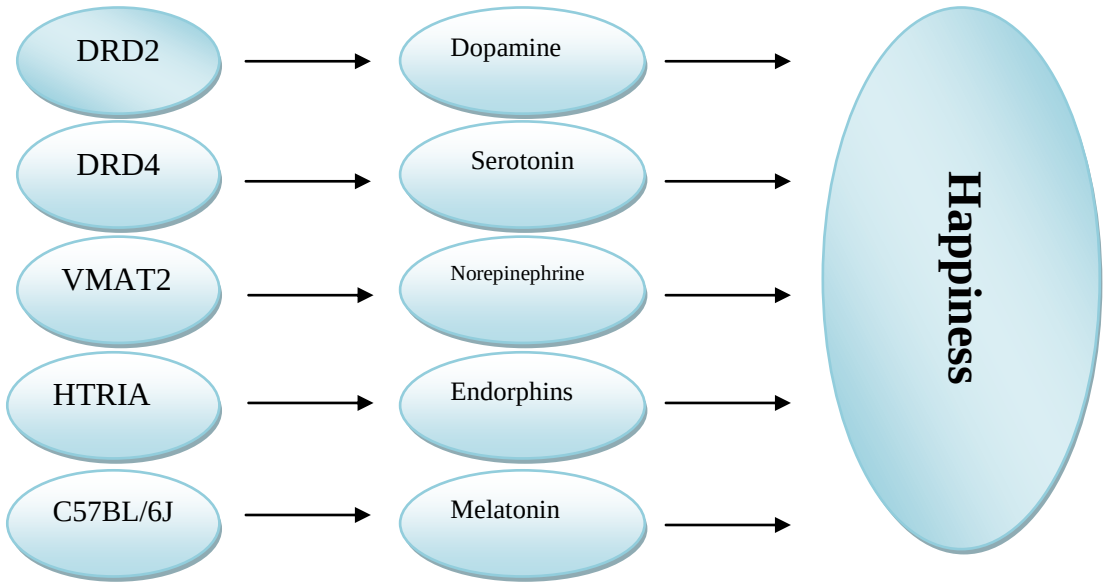

Fig. 1: Effects of genes on happiness neurotransmitters

Hormones and Endocrine glands

Endocrine glands with release hormones control various processes like growth, metabolism, and emotional regulation and so on. Endocrines included glands and other cells that produce hormone. In several studies, the role of some glands in regulating mood states indicated. Most related glands with mood states are pituitary and adrenal glands. Studies suggested that some released hormones from these glands have a fundamental role in happiness and mood regulation that explained in the following.

Cortisol

Hydrocortisone is a well- known Glucocorticoids in the body that is released from adrenal glands. This hormone release in response of inflammation or decrease the level of Glucocorticoid. This hormone regulate by CRH that release from hypothalamus and increase ACTH. ACTH increases Cortisol hormone. The role of this hormone in psychological process is managing stress. Several studies investigated the relation between Cortisol and depression as a contrary dimension of happiness.

Cortisol has been shown to be a consistent marker for depression. High levels of morning Cortisol

have been linkedto depression and neuroticism.Also, atypical Cortisol secretion patterns have been linked to depression, stress, and anxiety(27).Researchers, according to thesefindings, suggest that happiness related to level of Cortisol in the body. Is it a correct question?

Researches indicate that less salivary Cortisol is good predictor of happiness (28).

However, some researches directly investigated level of Cortisol on the body and its effect on happiness, findings showed that level of Cortisol is not a predictor of happiness (29). The relation of happiness and level of Cortisol needs to more studies.

Adrenaline

Adrenaline (also known as Epinephrine) is a hormone and a neurotransmitter that releases from Adrenal glands. Adrenaline has many functions in the body, regulating heart rate, blood vessel and air passage diameters, and metabolic shifts; Adrenaline release is a crucial component of the fight-or-flight response of the sympathetic nervous system.

Therefore, adrenaline produces similar effects to Cortisol, such as increased heart rate and immune system suppression. Researches indicate that urinary adrenaline is a good predictor of happiness (28).

Individuals with higher levels of "personal growth" and "purpose in life" registered lower and more stable levels of salivary Cortisol and urinary Adrenaline (28).

Oxitocin

Oxytocin is a peptide hormone that composed of nine amino acids (30).A hormone released from pituitary gland and control uterine spasms and breast feeding stimulus. Recently researches showed that Oxytocin causes a wide spectrum of behavioral and physiological effects mediated through receptors within the brain, such as maternal, sexual and social behaviors (31).Oxitocin facilitates the relationship with others and associated with positive social behaviors, so it assumes that related with happiness. While relationship has a strong effect on life satisfactory and there is a significant correlation between happiness and social relationship, then Oxitocin can be a mechanism that produces happiness through facilitating social relations (32, 33).

A biological model of happiness in presented in which one's genes, developmental history and basal physiologic state effect the release of OXT after a positive social stimulus. The change in OXT affects Happiness. The change in OXT also affects happiness directly via the HOME (Human Oxytocin Mediated Empathy) circuit (34)(Fig.2).

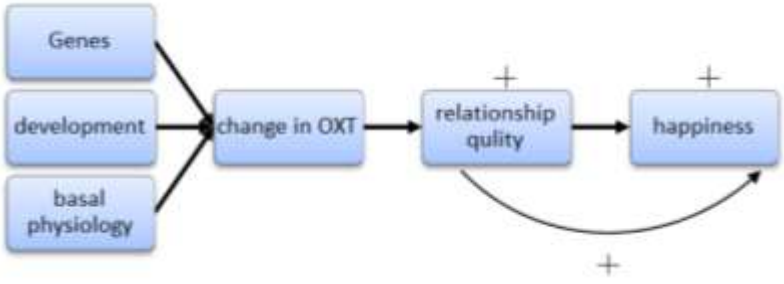

Fig.2: Effects of OXT on happiness

Physical health

Medicine and psychological findings showed that positive emotion reactions against life events can influence in various ways on physiologic characteristics. Therefore, several studies investigate the association between physical health and happiness. A group of researchers studied the general association between physical health and happiness and others investigate the relation between physical illness (hypertension, bulimia...) and happiness.

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Recently, several studies concluded that positive mood in individuals is a strong predictor of physical health an there is a significant correlation between positive mood and physical health (35-38). Researchers stated that people with happiness experience a long life (39). People with happiness behave healthier (weight control and practice) than others (40). Moreover, people with happiness inhibited the risky behaviors (37).

Having positive mood and happiness correlated with decreasing some illnesses such as hypertension, cardiovascular disease and fatness. Researchers find a strong relation between local of brain that manage weight and metabolism and areas that control cognition and emotions (41). Fatness is likely a risk factor for depression and then significantly decreases the quality of life (42).

Researchers indicated that rate of hypertension is low among happy societies (43).In addition, researchers concluded that special emotions like fear, anger and happy, play a clear and important role in psychopathology and treatment of cardiovascular diseases.

Recent studies showed that people with happiness can more fight with cancer and more survive. Some researchers used music therapy to increase positive emotions in individual with cancer; they conclude that music therapy has a significant effect on dealing with cancer (44). Van Dom 1989 described that positive attitudes can stop the serious disease and happiness is the best means against cancer (45). In addition, some researches indicated hypothesis of long life among happy cancers is invalid and some studies reported short life among cancers.

Typology and physical attraction

The first category of constitution, typology and physiognomy refer to Socrates. He divided humans into two distinctive categories: Habitus Apoplecticus, Habitus Phthisicus. New categories also formed based on mentioned category: Leptomorph = Ectomorph, pyknomorph = Endomorph and Athlet = mesomorph (46) (Fig. 3).

The relation between typology and mental and emotion characteristics or psychosomatic correlation involved a part of anthropology researches. For example, people with leptomorph style are sensitive, serious, manager, affective, optimism, intelligence introversion and vulnerable to schizophrenia, hypertension and ulcer. Based on studies assigned a group of signs to each type (46).

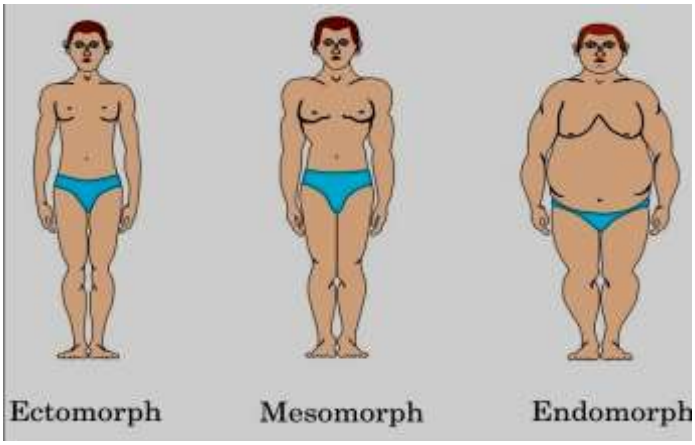

Fig. 3: Anthropometric typology

While the typology can form a specific emotion and behaviors, the image of our body can influence on this characteristics. It must be noted that imagination is affected by culture. Several studies investigate the relation between happiness and physical attractiveness and they found that there is a significant positive relation between them (46).

In social interaction, physical attractiveness leads tomany positive points. For example, other interested in choosing them as a friend, they are successful in choosing a partner, assessed by others positively and so on. Finally, it is important to know that there is a strong bias in assessing attractive people positively. Generally, attractive people perceived happier and successful than others (47). A Meta-analysis indicated that when people a person assessed as an attractive one, they assessed in comparison with non-attractive people more intelligent, kindly, socially and with more social skills (48). Bias to attractiveness is traceable in children. For example, teachers assess attractive children as lovely and intelligent students, unconsciously. This subject repeated in experimental condition and acquired same result.

Conclusion

Happiness is a new concept in positive psychology. Although, everyone uses this concept commonly as a clear concept, it has a complex meaning and composed of several factors. In ease, all effective factors divided into two dimensions: endogenic and exogenic. In spite of the influence of exogenic factors on happiness, endogenic factors form the basis of happiness. Biological factors as a part of endogenic factors, in ease, divided into five major areas: genetic factors, brain and neurotransmitters, endocrine glands and hormones, physical health and typology and attractiveness.

Twin studies suggested that genetic factors count for 35 -50 percent of happiness.

Recently studies have also focused on finding related genes in happiness. First, several genes identified in relation with mood and emotion and then among all mentioned genes, two genes suggested in relation with happiness: *5-HTTLPR* and *MAO-A*. We hope to clarify the genetic base of happiness in the future.

Brain studies have no clear findings about localization of happiness, but some part of brain introduced as emotion control centers: prefrontal cortex, amygdale, hippocampus, anterior cingulated cortex, and insular cortex. Neurotransmitters have no exact explain, but most related neurotransmitters in relation with happiness are as followed: endorphin, dopamine, serotonin, Nor-epinephrine, and melatonin.

Another factor that affected happiness in general is hormones and glands. Studies suggested that some released hormones (Cortisol, Adrenaline, Oxitocin) have a fundamental role in happiness and mood regulation.

Physical health and attractiveness also influence on happiness and they seem to be significant factor in comprising happiness

Finally, it can be said that genetic is all and other factors are additional. Based on special genetic structure, integrating related factors can result in happiness.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

Iranian Academy of Medical Sciences, Tehran, Iran supported financially this study. The authors declare that there is no conflict of interests.

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