Neuro-anatomy and neuro-physiology of happiness in ageing women

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ABSTRACT

Emotional lability is common after the menopause leading to significant unhappiness and deterioration in wellbeing of ageing women. Happiness results from the complex interplay of multiple endogenous and exogenous correlates which release "happiness hormones" and other neurotransmitters. These activate emotion centres in the brain resulting in a feeling of happiness and that of well-being. The emotional centres in the cerebral cortex and subcortical regions of the brain are connected by sophisticated limbic neural networks. This intricate network is controlled and stimulated by a number of neurotransmitters which are responsible for the integration, interpretation, formulation and the response to these correlates resulting in the perception of happiness. These neurotransmitters include oxytocin, dopamine, serotonin, endorphins, the "so-called happiness hormones" as well as gonadal hormones, gamma-aminobutyric acid, endocannabinoids and epinephrine which are the primary role players. The secretion of these hormones and neurotransmitters reflects interplay and/or interaction of one's environment, relationships, diet, exercise regime, and even one's gut microbes and the establishment of the sensation of happiness and well-being. Genetic makeup accounts for only 30-40% of one's happiness. This review article describes the interplay between the neuroanatomy, the complex interlacing neural network and the neurotransmitters which are impacted by external factors.

KEYWORDS

Happiness, ageing women, neurotransmitters, neurohormones.

Introduction

"*Everything should be made as simple as possible, but not simpler.*"
Albert Einstein.

During the perimenopausal, menopausal and postmenopausal transition, women commonly complain that emotional lability causes significant deterioration in their wellbeing, resulting in obviously perceived unhappiness. The natural and common response by medical attendants is that the prevailing mood is due to estrogen deficiency and hence hormonal therapy is usually prescribed. Although acceptable, this is not, and should not, be seen as the only management strategy.

Much has been written about the human brain and emotions over the last 30 years, which results in a vast reservoir of complicated information that is challenging to decipher, translate and understand. From an evolutionary perspective, emotions seem to have been developed to help humans solve problems. Emotions are useful, they motivate us to engage in actions important for survival—actions such as foraging for food, seeking shelter, choosing mates, guarding against predators, and predicting behaviours. The emotion of happiness, which encompasses sensations of feeling joy, and contentment, is fundamental to our sense of wellbeing and our ability to cope adequately.

The origin, formulation, interpretation and response to the sensation of happiness involves the interactions of many multifaceted endogenous and exogenous cognitive appraisals, along with simple programs embedded in our genes and our brains. All emotions originate in the brain's limbic system and individuals tend to be the happiest when their limbic system is relatively inactive, reporting more positive than negative emotions. When the limbic system is highly activated, negative emotions such as anger and guilt may override positive responses such as joy and happiness. Generally, the limbic system provides the means through which different type of events can be interpreted [1]. During the perimenopause and after the menopause, emotional lability among ageing women is a common complaint leading to varying degrees of unhappiness and impaired quality of life. As stated above, medical health providers will invariably prescribe hormonal or antidepressant therapy as the "quick" fix, in the hope that these women will find happiness and contentment. This article provides a brief overview of the complex innate natural pathways responsible for happiness and the role ageing women can play in facilitating natural strategies

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to stimulate happiness and contentment other than simply taking medications to confront the problem.

WHAT IS HAPPINESS?

"Happiness "is not easy to define. It is known to be a complex emotion which is composed of several endogenous and exogenous components, all of which play a role in its expression. Happiness consists of two basic concepts: a state of mind and a state of well-being [2].

It is typically determined by three primary factors

(a) **Life's satisfaction**: positive emotions based on past, present and projected future experiences.
(b) **Engagement in daily activities:** whether at work, in relationships, or during leisure time.
(c) **Having meaning and purpose in life:** short- and long-term goals and aspirations [3].

Happiness has two subjective appreciations.

a. Hedonia, sole pleasure, a state of mind or short-term fleeting kind of happiness, most often associated with having a good time.

b. Eudaimonia, a life well lived resulting in feelings that are pleasurable and are subjectively appreciated as significant. It is obtained by people striving to achieve goals through activities that offer less pleasure on a day-to-day level but provide a sense of strong satisfaction in the long run. This provides the most protection from illness, disease, emotional and psychological distress [4,5].

In the absence of external threats or stressors, the natural state of a healthy mind is one of contentment — so-called "default contentment". People are inclined to be more optimistic, more happy than sad, but contentment and happiness require a healthy mind [6].

There are, however, exceptions to the rule. Some adults are grumpier than others, especially those who face progressive physical and cognitive decline, chronic stressors, health issues or loss of social belonging, all these being risk factors that become more prevalent with age [7]. On average, emotional experiences become rather more positive than negative with advancing years because of changes in one's environment [8]. Aging in adults has an enhancing effect for recalling positive information, in contrast to the age-related decline in cognitive functioning [9].

People will vary in their reactions to emotional challenges [10]. Those with greater activity in their left frontal cortex tend to be happier and more optimistic and show greater positive affect than those whose right frontal cortex is more active [11]. Happier people tend to maintain a better-quality of well-being by regulating undesirable emotions more effectively [12]. The greater the connection to one's core values and to the core values of close friends, the greater the chance for continued optimism [13].

Generally, the natural mechanisms that trigger happiness can be activated by the following factors [14]:

- Supportive relationships
- Material and physical security
- A sense of meaning or purpose
- Engagement in interesting and challenging activities
- Independence
- Religion
- Trust
- Helping others
- Achieving goals
- Employment
- Connection with the natural environment

Neuroanatomy

Happiness comes about through the interplay of a multitude of endogenous and exogenous correlates that release a number of "happiness hormones" and other neurotransmitters which activate the emotion centres in the brain, resulting in the feeling of happiness and that of well-being. The emotional centres in the cerebral cortex and subcortical regions of the brain are connected by the complex limbic neural network, an elaborate network of interlacing neural pathways.

The specific components of the brain responsible for affective and effective responses are multiple, complicated and interconnected. There is no single defined area of the brain to account for the localization of happiness other than for those centres responsible for emotion control. These areas include the prefrontal cortex, amygdala, hippocampus, cingulum, and the insula. The prefrontal cortex plays a major role in emotion-processing and it appears that the prefrontal cortex manages goals and the way we achieve them, acting as a kind of working memory for affect and thought to play a role in evaluating reward versus punishment [15]. Other important areas include the accumbens nucleus (the part of basal ganglia) and brain stem which are believed to be involved in reward and reinforcement. Many neurological connections running both ways between cortical areas and subcortical areas (including the amygdala), constitute the limbic system [16]. The hypothalamus links the nervous system to the endocrine system which produces hormones that are key mediators of mood and emotion. The neuronal network transmits dopamine signals from the ventral tegmental area to the limbic system and the prefrontal cortex. The amygdala is involved not only in negative emotions such as fear, but also in positive emotions. Indeed, the amygdala is considered the "heart and soul" of the brain's emotional network [17].

Neurotransmitters

The intricate network of cerebral centres, neurones, neural tracts and synaptic junctions, is constantly analysing positive and negative emotions, formulating interpretation and producing a response. The brain is "wired" for endogenous and exogenous messages and is responsible for the behavioural and emotional responses. The transfer of all the messages within this network is by means of neurotransmitters, hormones and other mechanisms. The most important neurotransmitters include not only the "four happy hormones, "oxytocin, serotonin, dopamine and endorphins", but also gamma aminobutyric acid (GABA), norepinephrine, epinephrine, female gonadal hormones and endocannabinoids. Melatonin may also play a role through its impact on sleep [18].

Oxytocin

Known as the "cuddle" hormone, oxytocin is the neurochemical that has allowed humans to become social creatures. It is responsible for the feeling of empathy, it makes one feel closer to others by encouraging social bonding [19]. Oxytocin regulates emotional responses and behaviours and stimulates socialising, trust, empathy, gazing, positive memories and upbeat communication [20]. The greater the engagement in these feel-good behaviours is, the more oxytocin is secreted. Oxytocin facilitates bonding with children, increases romantic attachment, and plays an important role in reproduction for both sexes [21], but can also lead to negative emotions such as jealousy or suspicion [22]. Romance, caring relationships, touching, friendship and cuddling pets can increase oxytocin release.

Dopamine

Dopamine is identified as the "pleasure hormone" and is released when one strives towards a goal [23]. It is involved in many pathways in the brain, including movement, sleep, learning, mood, memory, and attention. It keeps one alert, focussed and motivates one to complete the planned project, including achieving the satisfaction of reaching one's goal [24]. Setting daily or monthly goals raises the level of dopamine, although achieving goals increases not only dopamine, but also serotonin and endorphins. Dopamine is often considered to be the neurochemical most strongly associated with happiness. It may also be responsible for reward-driven behaviour and pleasure-seeking activities, such as behaviour resulting in the sensation of pride, satisfaction after eating comfort food or achieving an improved body shape or weight goals [25].

Serotonin

Butyrate and acetate, the building blocks of the serotonin precursor, tryptophan, have been proven to increase serotonin production, 90% of which is produced in the gut. Tryptophan is primarily obtained from diet. Serotonin is very effective in preventing depression and as a result triggering happiness feeling. The composition of one's diet plays an important role in fostering the right gut microbiome flora that produces acetate and butyrate. A balanced whole-food diet, rich in fibre and only moderate amounts of fats and red meat increase serotonin level [26]. Regular exercise boosts mood, relieves anxiety, and even combats depression by promoting tryptophan and serotonin levels and enhancing diversity of the gut microbiome [27]. Foods that are associated with increasing serotonin levels include apples, citrus, mushrooms, barley, oats, beetroot, cranberries, onions, berries, garlic, rye, blackberries and Jerusalem artichoke. Foods rich in tryptophan include chickpeas, quinoa, spirulina, soybeans, milk, cod and salmon, butter, egg yolks, fish, turkey, almonds, dried dates, bananas and cottage cheese [28].

Endorphins

Endorphins, "the pain-killing molecules," have analgesic properties. They are produced by the pituitary gland and hypothalamus during strenuous physical exertion, especially during high intensity anaerobic cardio and strength training, sexual intercourse, and orgasm [29]. They are our body's natural painkillers, pain blockers, and are responsible for our feelings of pleasure. Endorphins are strongly associated with the fight-or-flight response and play an important role in alleviating depression. Other ways to increase endorphin levels include listening to music or eating spicy foods [30].

Gamma-aminobutyric acid (GABA)

The "anti-anxiety molecule", GABA, is the chief inhibitory neurotransmitter in the developmentally mature mammalian central nervous system and is produced from glutamic acid. It slows down the firing of neurons and activity of the limbic system to reduce fear, anxiety and panic, creating a sense of calmness; in other words, it is a natural tranquilizer. Factors that enhance GABA release include zinc intake, yoga, meditation and the use of benzodiazepines [31].

Female gonadal hormones

Receptors for estradiol, progesterone and testosterone are present throughout the brain, including the cortical areas, although the largest numbers are found in the hypothalamus and other parts of the limbic system. Estradiol and progesterone act through these receptors whilst the progesterone metabolites also interact with the GABA system [32]. The gonadal hormones modulate serotonin neurons, influencing serotonergic neurotransmission at several levels by controlling synthesis and degradation of serotonin. They also regulate dopaminergic and noradrenergic neurotransmission. High endogenous levels of testosterone suppress activity in prefrontal brain regions suppressing communication between the prefrontal brain and the amygdala, increasing chances of aggression, depression, impulsivity, anger, mood swings and reduced levels of empathy [33].

Endocannabinoids

The endocannabinoid system involves three core components: endocannabinoids, receptors, and enzymes. The two key endocannabinoids are anandamide and 2-arachidonoylglyerol. Anandamide, recognised as the "bliss hormone," is a naturally occurring chemical that attaches to the same brain cell receptors as does marijuana's active ingredient, delta-9-tetrahydrocannabinol. The key receptors are the CB1, found mostly in the central nervous system, especially in the frontal cortex, hippocampus, cerebellum and basal ganglia, and CB2 receptors found mainly in the peripheral nervous system, especially immune cells. Endocannabinoids can bind to either receptor and the effects depend on where the receptor is located and to which endocannabinoid it binds. Circulating endocannabinoids are stress-responsive and their primary role is to restore body homeostasis after stress. They impact on serotonergic, dopaminergic and GABA neurotransmission resulting in improved moods, particularly reducing depression, anxiety and alleviating pain. Genetic disorders which cause low levels of the enzyme which is responsible for breaking down endocannabinoids will result in high levels of anandamide and constantly better moods, levels of happiness, and a general sense of well-being. Sources for endocannabinoids include exercise, dark chocolate, black truffles, omega 3 and kaempferol [34].

Epinephrine

Epinephrine is "the energy molecule". It plays an important role in the fight-or-flight mechanism. Release is exhilarating and

creates a surge in energy, causing an increase in heart rate and blood pressure. Epinephrine causes less important blood vessels to constrict and increases blood flow to larger muscles. It makes one feel very alive. Epinephrine can be an antidote for boredom, malaise, and stagnation [35].

Genetic factors

Studies of twins have suggested that genetic factors account for about 35-40% of happiness. Two genes, *5-HTTLPR* and *MAO-A-L* have been shown to be linked to emotional responses. An association has been described between genes and life satisfaction as a cognitive dimension of happiness [36]. They code for serotonin distribution in brain cells and therefore lead to mood regulation. Alleles on these genes may be a risk factor for stress-related negative consequences such as alcoholism aggression and antisocial problems [37].

Some gender differences in happiness do appear to exist. Women, compared to men, have an increased likelihood of experiencing intense, uplifting emotions such as joy and happiness. Women are more likely to express happiness, warmth and fear, which help with social bonding, whereas men display more anger, pride and contempt, emotions which tend to support a protector and provider role [38].

Ways to increase natural secretion of the four "happy hormones" [39]

- Exercise
- Taking part in fulfilling activities
- Socializing with friends, family
- Setting and meeting goals consistently
- Sunlight
- Eating dark chocolate and foods high in tryptophan
- Playing with pets
- Hugging, kissing and touching
- Meditation (decreases cortisol, increases endorphins)
- Sexual activity

Conclusion

There is much more to happiness in ageing women than only taking hormonal therapy and/or antidepressants. Hormonal therapy does impact directly and indirectly on improving emotional lability, but it is important to realise that hormonal therapy will primarily address only one mechanism within the very complex neurological network responsible for the promotion of happiness, joy and contentment. Hormonal therapy will also very likely improve indirectly the latter emotions by suppressing vasomotor symptoms, improving sleeping and improving vaginal dryness. But treatment of menopausal symptoms should not be undertaken in a vacuum. Women after the menopause should be advised that there are a number of strategies which either on their own, or in combination with hormonal therapy, will improve the clinical wellbeing substantially. Happiness in the ageing woman relies on the interplay of a multitude of endogenous and exogenous correlates which release a number of "happiness hormones" and other neurotransmitters which activate the cerebral emotion centres and result in the feeling of happiness and improved well-being. The secretion of these happiness hormones and other neurotransmitters is a reflection of an ageing woman's environment, relationships, diet, exercise regime, and, in some cases, even one's gut microbes.

In summary, the ageing woman's attitude to life's challenges, as well as her choices to incorporate simple ways to facilitate the secretion of appropriate hormones, and her response to unpleasant experiences, can have a big impact on attaining happiness.

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