Special article

Beauty and health: an intriguing liaison?

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ABSTRACT

The exposure to different form of beauty coming from visual art, music, nature, architecture, improves mental health and exerts neurotrophic effects on different parts of the brain. This in turn improves physical health, prolongs life expectancy, and reduces the risk of serious degenerative diseases such as Alzheimer's and cancer. These beneficial actions would not be understandable and plausible if one did not accept the mind-body unity. The 'hegemonic' role of the brain in health and illness can be discerned, for example, in the effect of emotions on vital physiological parameters, in the relationships between stress and many medical-clinical pathologies, in the control exercised by the brain over the immune system reflecting also in the inhibition of tumour progression.

Introduction: how beauty entered science from philosophy and literature

In a world dominated by economics and finance, beauty is often considered secondary, futile, or even useless. For many centuries instead, beauty was the domain of philosophers and writers. Plato is the first to attribute to beauty an autonomous existence, detached from other values, such as justice and goodness. In Phaedrus, his most famous work, there are many quotations dedicated to beauty (1).

"If ever a moment deserves to be experienced, this is the one you experience when contemplating beauty itself".

"When you see the beauty down here, you are reminded of true beauty, then you put on your wings and wish to soar".

For St. Augustine, beauty is the testimony of God's existence (2).

"Ask the beauty of the earth, the beauty of the sea, the beauty of the air diffused and suffused. Ask the beauty of the sky, in the order of the stars, the sun, which with its splendor illuminates the day; ask the moon, which with its glow moderates the darkness of the night. Question them! They will all answer you: Look at us: we are beautiful! Their beauty makes them known. This changeable beauty, who created it, if not the Immutable Beauty?".

While for Leibniz beauty is something we simply are not able to define; for David Hume: *"Beauty is not a quality of the things themselves: it exists only in the mind that contemplates them and each mind perceives a different beauty"* (3).

This concept was shared by Johann Wolfgang Goethe who had to say: *"Beauty is in the eye of the beholder".*

As we will see the matter of subjective nature of the sentiment of beauty has been the key to understand the biological basis of this kind of emotion.

Famous writers dedicated to beauty important meditations: for the Italian poet Ugo Foscolo:

"Beauty is a kind of visible harmony that sweetly penetrates human hearts".

What about Fëdor Dostoevskij? His famous quote: *"Know that mankind can do without the English, that it can do without Germany, that nothing is easier for it than to do without the Russians, that it needs neither science nor bread to live, but that only beauty is indispensable to it, because without beauty there will be nothing left to do in this world . . ."*

According to Oscar Wilde *"Beauty is the only thing against which the force of time is in vain. Philosophies disintegrate like sand, beliefs succeed one another, but what is beautiful is a joy for all seasons, and a possession for all eternity".*

After philosophers and writers, the first scientists becoming interested in beauty were mathematicians and physicists. The famous mathematician Jules Henri Poincaré, pointed out in this way the

relationship between science and beauty (4): *"The scientist does not study nature because it is useful to do so. He studies it because he derives pleasure from it; and he derives pleasure from it because it is beautiful. If nature were not beautiful, it would not be worth knowing and life would not be worth living. I mean to refer to that intimate beauty that derives from the harmonious order of the parts and that can be grasped by a pure intelligence"*.

Another famous mathematician, Bertrand Russell, had to say: *"Properly observed mathematics expresses not only truth but also supreme beauty"* (5).

With the physicist Paul Dirac never had the role of beauty been so central to the history of the scientific enterprise (6). *"There is only one rock that can survive any storm and to which we can cling tightly: the idea that the fundamental laws of Nature are expressed by a mathematically beautiful theory"*.

"A theory that includes mathematical beauty is more likely to be right and correct than an unpleasant theory, even if confirmed by experimental data". *mathematically beautiful"*

Another giant scientist, Hermann Weyl, in 1918, after Einstein had already devised his general theory of relativity, which replaced Newton's theory of gravity, tried to unify it with Maxwell's theory of electro-magnetism. His idea was a splendid example of mathematical work, but unfortunately, as Einstein himself pointed out, his effort contradicted the reality of physics. Nevertheless, Weyl's mathematical calculation was published with an objection written by Einstein in the appendix. A few years after quantum mechanics appeared in the scientific field, Weyl's original idea was slightly modified and accepted. Thus, while today Einstein's objection has lapsed, Weyl's theory has been has become the basis on which all subsequent work in theoretical physics has been postulated. Had Weyl abdicated his convictions and not instead insisted that his mathematical work be published anyway, physics would never have evolved. He once said: *"In my research I have always tried to combine the true with the beautiful; but when I have had to choose between one and the other, I have usually chosen the beautiful"* (7).

Seeking the "beauty centre" in the brain

At the end of the last century, other scientists, mainly neurophysiologists, began to ask questions about beauty: Why have beauty and art had such a prominent presence in all societies? Why has mankind desired to be surrounded by beauty since ancient times? Why do we attribute so much 'value' (cultural, social, economic) to the possession and enjoyment of a 'beautiful' product? What are the biological bases of this 'value'?

The pioneer neuroscientist Samir Zeki highlighted how the sight of a figurative work that contains elements of great beauty, such as Ingres's Big Odalisque, manages to activate a special area of the brain, which he named the centre of beauty, while a work that contains elements of 'ugliness', such as Lucian Freud's Big Sue, activates different areas that we might call centre of ugliness. In a famous experiment, Kawabata and Zeki (8) asked participants with no experience in art to make aesthetic judgements of paintings by categorising them as ugly, neutral, or beautiful. Regardless of the category of painting being viewed (*e.g.* abstract, landscape, portrait, still life), the authors found the orbito-frontal cortex to be more engaged when participants perceived paintings rated as beautiful compared to ugly. In a similar vein, Vartanian and Goel (9) found that while activity in bilateral occipital gyri, left cingulate sulcus, and bilateral fusiform gyri increased with increasing subjective preference attributed to a series of paintings, the activity in right caudate nucleus, a brain region implicated in reward processing, showed a similar pattern. Thus, brain activity appeared to be modulated by the affective value each viewer associated with individual paintings, suggesting a neurobiological response related to the hedonic value of an artistic stimulus. A new discipline waw born and was named by Zeki Neuro-aesthetics.

Later on, The Zeki beauty centre, located in the orbitofrontal cortex, resulted to be activated by different form of aesthetic stimuli: from beautiful music, to particular scents, to the sound and sight of running water, and even to particular taste stimuli. Even natural man-made landscapes (gardens, fountains, and pleasant places) always activate the same area. (10-12). The follow-up work from the same group showed that for mathematicians viewing beautiful mathematical formulas also activated the mOFC (Zeki *et al*., 2014). Based on these results, Ishizu and Zeki concluded that there is a universal neural characteristic associated with the experience of beauty.

The discovery of Zeki that our brain is evolved to be able to appreciate anything that has this capacity to be perceived as beautiful, triggered many studies focusing the common neural basis of the experience of beauty. A metanalysis reviewed 49 studies carried out in the last two decades to address this task (13). The message emerging from this metanalysis confirmed that the beauty of visual art convergently activated the anterior medial prefrontal cortex (aMPFC) while the beauty of faces convergently activated the left ventral striatum.

Some studies like that published by Mastrandrea *et al*. (14), aimed to assess, through physiological measurements such as blood pressure and heart rate, whether exposure to art museums and to different art styles (figurative *vs*. modern art) was able to enhance visitors' well-being in terms of relaxing and stress reduction. Seventy-seven participants were randomly assigned to one of three conditions, on the basis of the typology of the art style they were exposed to in the museum visit: (1) figurative art, (2) modern art and (3) museum office (as a control condition). Blood pressure and heart rate were measured before and after the visits. Most of the participants exposed to figurative art significantly decreased systolic blood pressure compared to those exposed to modern art and museum office. These findings suggest that museum visits can have health benefits, and figurative art may decrease systolic blood pressure.

If our brain has a natural attraction for beauty, this would imply that something happened in the evolution from hominids species to homo sapiens. An

orthodox view is that there is an essential connection between beauty and art; where there is art, there is beauty.

Homo sapiens and beauty

We do not know how art originated. What we do know, however, is that thirty to forty thousand years ago, during the final phase of the Paleolithic period, human beings were well aware of the value of images and figurations. This is demonstrated by ancient evidence of 'rupestrian' painting, so called because it was created on the rocky walls of certain caves.

Our ancestors, inhabiting areas such as Southern France that at the time offered a desolate and cold tundra-like landscape, spent a large part of their existence in gloomy places such as the Chauvet cave or the Lascaut cave, mainly to defend themselves from ferocious animals. What drove them to draw harmonious animal figures on the rock? Religious sense, magical practices, self-affirmation, a sense of belonging to a social group? Perhaps. No one can know unfortunately. But why not think more simply that they painted these beautiful forms for the sheer pleasure of admiring them, of decorating their homes, of expressing their own sense of aesthetics and deriving happiness from this beauty? It was precisely through the language of art that man was able to bear witness to his presence and thus affirm his own self in an extremely harsh environmental context; he was able to tell of his life and transmit information, in the absence of writing; he was able to give face and body to that reality, perceived as supernatural, that was mysterious and obscure to him; he was able to celebrate a beauty that he recognised in everything around him. The stylisation of bison, giraffes, lions, horses, which can be admired in numerous prehistoric paintings and graffiti, seems to belong, precisely, to the category of 'beauty for beauty's sake', or, in certain cases, seems to spring from that quest for expressionistic essentiality that has led modern art from a certain 'naive' naturalism to the increasingly abstract and rarefied forms of the informal, passing through the subjective feeling of the artist.

But what ties us inextricably to the beauty of natural environment? The key to understanding this instinct is our "biophilia" that is an innate affinity of life or living systems, a concept introduced by Edward Osborne Wilson, the famous American entomologist considered the contemporary Darwin, who passed away in late 2021 (15). Repeatedly cited in trade journals as one of the world's most influential scientists and intellectuals, he dedicated himself to the conservation of the planet until the end. Wilson uses the term in a related sense when he suggests that biophilia describes "the connections that humans unconsciously seek with the rest of life". He proposed the possibility that the deep affiliations humans have with other life forms and with nature are rooted in our biology. Greater affiliations to natural elements than to artificial objects are evidence of biophilia. It seems therefore that human beings instinctively seek beauty mainly because beauty can generate happiness and psychological well-being.

Molecular mechanisms underlying the medical effects of beauty

Although specialised brain centres like the orbitofrontal cortex respond to aesthetic reward, the real core of the reward system is represented by the cortical-basal ganglia circuit (16).

The key structures in this network are the anterior cingulate cortex, the ventral striatum, the ventral pallidum, and the midbrain. In addition, other structures, including the dorsal prefrontal cortex, amygdala, hippocampus, thalamus, and lateral habenular nucleus, and specific brainstem structures such as the pedunculopontine nucleus, and the raphe nucleus, are key components in regulating the reward circuit. The connectivity between these areas forms a complex neural network that mediates different aspects of reward processing.

These structures are ancient at an evolutionary level and, when activated, bring into play neuro-mediators like dopamine, to which we owe the various sensations of peace, contentment, and pleasantness that we experience when we appreciate beauty. In the brain first, and then throughout the body, molecules such as dopamine, oxytocin, serotonin, and endorphins are in fact put into circulation, each of which can interfere in various ways with anxiety, stress, depression. These are precisely the mediators to which the salutogenic effects of beauty are attributed.

The most important neuro-mediator is dopamine, to which we attribute the greatest salutogenic effects related to experiencing beauty, such as the sensation of pleasantness, fulfilment, reward, and the classic shiver down the spine when listening for example to a piece of music that moves us.

Numerous neuroimaging studies (PET and fMRI) attest that aesthetic experience activates brain structures rich in dopaminergic neurons, such as the nucleus accumbens, hippocampus, substantia nigra and ventral tegmental area (VTA) (17).

Among the arts, music is certainly the most studied in relation to health. The summary of studies attesting to the contribution of dopamine in musical pleasure has been highlighted in the review by Chandra and Levitin (1) where are listed very sophisticated studies conducted on both musicians and non-musicians. The target is the increased blood flow in dopaminergic areas because of listening to music. Dopaminergic activity is also connected with pain modulating effect, which explain how listening to beautiful music can exert analgesic effects (18).

Another chemical compound intervenes in the mechanism of action. This is oxytocin, a neuropeptide produced by the hypothalamus and secreted by the pituitary gland. This neurohormone comes into play heavily in the phases before and after childbirth, but its physiological actions also affect social relationships and empathy, that is why it has been called the friendship hormone. Oxytocin exerts many physiological functions. It promotes maternal and paternal emotional behaviour, promotes social relationships and empathy, promotes affective-sexual behaviour has anxiolytic, anti-stress, antidepressant activity and lastly modulates states of consciousness (19). Beyond salutogenic effects, such as empathy, sharing and friendship, oxytocin also modulates the pain

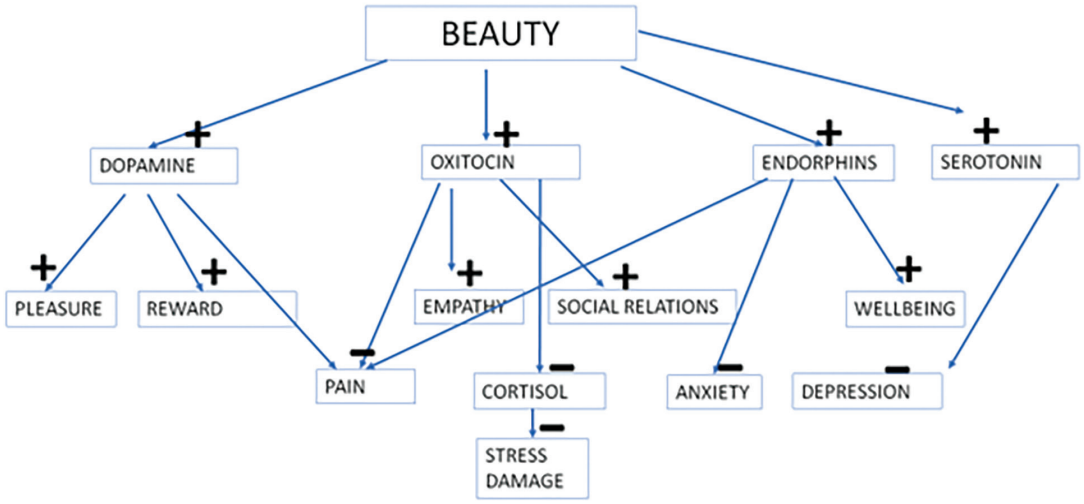

Fig. 1. Salutogenic effects of beauty exposure.

experience. A number of studies attest its analgesic effect in acute and chronic pain (20). But oxytocin has another fundamental action and that is to attenuate cortisol secretion, probably through an inhibition of ACTH.

This appears to be the mechanism by which aesthetic experience contrasts the bad consequences of stress. A meta-analysis consisting in 18 randomised placebo-controlled studies has considered the acute effect of intranasal administration of oxytocin on the inhibition of cortisol response to stressful stimuli (21). Overall, oxytocin administration showed a greater attenuation of the cortisol response to laboratory tasks that strongly activated the HPA axis. The effect was more robust in sick subjects than in healthy volunteers, suggesting a possible greater sensitivity to oxytocin among those with a clinical diagnosis.

The principal neurochemical mechanisms involved in the salutogenic effects of beauty experience are shown in Figure 1.

How the brain commands the body through reward circuits

In the late seventies of last century, George Engel, a New York physician specialised in internal medicine, influenced by Boston psychiatrist John Romano, proposed the bio-psycho-social model, the basic assumption of which is that health and illness are consequences of the interaction between biological, psychological and social factors, publishing this manifesto in the journal *Science* (22).

Engel decided to elaborate this new model 'so that it would become a conceptual framework to guide physicians in their daily work with patients', as well as to have a broader scientific understanding of what Engel calls the 'human domain'; the aim was to create a model that would act as a general framework to direct theoretical and empirical exploration not only towards an understanding of processes or diseases, but also towards an understanding of the human dimension as a whole. And one of the four pillars of the bio-psycho-social model highlighted by Engles is that mind and body are not separate.

To date, a considerable amount of clinical-experimental data has proven that this assumption is true. For example, stressful conditions, whether related to life events or to chronically stressful events, can favour the onset of somatic diseases (23).

In the cardiovascular field, the paradigm is Tako-Tsubo Syndrome, also known as 'Broken Heart' Syndrome. It was identified in the early 1990s as a new clinical entity, with an onset typical of that of a myocardial infarction (24). This pathology is triggered by intense psychological stress (strong emotions, fear, panic, fright, bereavement), with a prevalence in females.

Characteristic of this form is the transient balloniform modification of the left ventricular apex, probably due to stimuli of neurogenic origin, originating from prolonged physical or emotional stress. This deformation, visible with imaging techniques such as echocardiography or magnetic resonance imaging, causes the left ventricle to take on the shape of a basket (tsubo) used by Japanese fishermen to catch octopus (tako), hence the name.

Advanced imaging methods have greatly facilitated the evaluation of the pathological mechanisms linking stress to human diseases (25-26).

External stressors activate the brain's salience network, a group of interconnected structures within which the amygdala, a limbic structure, plays a critical role. The amygdala's resting metabolic activity (AmygA) can be quantified using 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT), providing a physiologic measure that associates with anxious temperament in animal models (27).

Resting metabolic amygdalar activity, measured at the time of cancer staging, is a significant predictor of survival among patients with head and neck cancer. AmygA, quantified on routine 18F-FDG-PET/CT images obtained at cancer staging, independently and robustly predicts mortality and cancer progression among patients with HNCA (28). Future studies should test whether strategies that attenuate AmygA such as art therapy, may improve cancer survival.

Recently, scientists like Asya Rolls, a neuroimmunologist at the Technion – Israel Institute of Technology in Haifa, have discovered that a specific region of the brain, called the ventral tegmental area, involved in positive emotion and motivation can influence healing

of experimental myocardial infarction (29). This study has its roots in decades of research pointing to the contribution of a person's psychological state to their heart health (30).

It is well known that among women with breast cancer, those who underwent supportive group therapy and self-hypnosis in addition to routine cancer care survived longer than those who received only the latter. Several other studies have documented a similar link between survival and the mental states of people with cancer (31). It is noteworthy that activating neurons in the VTA noticeably shrank the cancer (32).

It has been almost 60 years since it was first hypothesised that emotions could influence the function of the immune system (33). Now we know that there are multiple types of communication between the brain and the immune systems. For example, a direct link between them was discovered through the lymphatic vessels in the meninges. This discovery of the central nervous system lymphatic system may call for a reassessment of basic assumptions in neuroimmunology and sheds new light on the aetiology of neuroinflammatory and neurodegenerative diseases associated with immune system dysfunction (34).

Another recent contribution confirms the direct link between the central nervous system and the immune system, highlighting the distribution of sympathetic nerve endings in the lymph nodes. The study showed how human lymph nodes contain sympathetic nerves in their capsule, trabeculae, cortex, medulla and hilum, both as paravascular and as discrete structures. The presence of discrete structures in relation to T cells and non-T cell-rich areas suggests neural regulation of structures other than blood vessels, which was further supported by the presence of varicosities in a portion of these nerves. These observations are of relevance in further understanding neural regulation of lymph node immune responses and in the development of neuromodulatory immune therapies (35).

Studying plaque formation in the arteries, a European research team including Italian scientists has revealed an unexpected connection between the circulatory, nervous, and immune systems. Besides suggesting that atherosclerosis might be partly controlled by the brain, the study reveals that the interaction between immune cells and nerves in the outermost layer of artery walls modulated the progression of atherosclerosis, a biological mechanism that could play a role in many other diseases (36).

Conclusion

Medical doctors should appreciate the emerging role of beauty experience in shaping mental and physical health at very low cost and without side effects. An especially promising avenue of research in this vein is the investigation of the reward systems associated to aesthetic experience, which have been so far mainly studied with reference to music listening but which have to do with many other forms of beauty linked to visual arts, literature, the natural environment and architecture.

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