Empathy, Medicine and Society

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Master's thesis / Diplomski rad

2021

Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj: **University of Zagreb, School of Medicine / Sveučilište u Zagrebu, Medicinski fakultet**

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:599687

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Download date / Datum preuzimanja: **2025-02-09**

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Graduation Thesis

Zagreb, 2022.

This graduation thesis was written at the Department of Psychiatry, Clinical Hospital Centre, Zagreb, mentored by Izv. prof. dr. sc. Marijana Braš and was submitted for evaluation during the academic year 2021/2022.

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Abstract:

The current article is an integrative literature review on the concept and meaning of empathy in society and in medicine. Empathy can be conceptualized as the ability to understand and share in others' emotions while maintaining a distinction between self and others. It makes a difference in our every day relationships and it is considered one of the fundamental elements in the formation and maintenance of social groups, and it drives many aspects of social behavior such as moral sense, child care, and prosocial behavior towards relatives and even complete strangers. This human trait has contributed to the cognitive, linguistic, cultural, social, and technological evolution of the human species. Functional neuroimaging (fMRI) studies of health workers, which examine brain activation patterns in response to empathy-eliciting situations, bring theoretical clarity to the neurocognitive processes underlying emotional and cognitive empathy, interpersonal sensitivity, and caring. Empathetic differences have been observed between sexes, ages, cultures, and interpersonal relationships. The mechanisms underlying the phenomenon of empathy may be related to neural circuits that are activated relatively independently but often interact. These circuits are deeply interwoven in the fabric of the brain. It is well known that empathy plays a critical role in the doctor-patient relationship and has a favorable effect on health outcomes. Currently, there is an issue with the balance between scientific-technical and psychosocial aspects of patient health care.
The lack of empathy education, the emphasis on treatment within the current academic culture, the high number of patients that doctors must handle, and also the lack of adequate time are all factors that negatively influence the development of empathy.

Keywords: empathy, social interaction, neurobiology, doctor – patient relationship.

Sažetak:

Ovaj članak je integrativni pregled literature o konceptu i značenju empatije u društvu i medicini. Empatija se može konceptualizirati kao sposobnost razumijevanja i dijeljenja tuđih emocija uz održavanje razlike između sebe i drugih. To čini razliku u našim svakodnevnim odnosima i smatra se jednim od temeljnih elemenata u formiranju i održavanju društvenih skupina, a pokreće mnoge aspekte društvenog ponašanja kao što su moralni smisao, briga o djeci i prosocijalno ponašanje prema rodbini, pa čak i potpunim strancima. Ova ljudska osobina pridonijela je kognitivnoj, jezičnoj, kulturnoj, društvenoj i tehnološkoj evoluciji ljudske vrste. Funkcionalne neuroimaging (fMRI) studije zdravstvenih radnika, koje ispituju obrasce aktivacije mozga kao odgovor na situacije koje izazivaju empatiju, donose teorijsku jasnoću neurokognitivnim procesima na kojima se temelje emocionalna i kognitivna empatija, međuljudska osjetljivost i briga. Empatične razlike uočene su između spolova, dobi, kultura i međuljudskih odnosa. Mehanizmi na kojima se temelji fenomen empatije mogu biti povezani s neuronskim krugovima koji se aktiviraju relativno neovisno, ali često međusobno djeluju. Ti su krugovi duboko isprepleteni u tkanini mozga. Poznato je da empatija igra ključnu ulogu u odnosu liječnika i pacijenta i povoljno utječe na zdravstvene ishode. Trenutno postoji problem s ravnotežom između znanstveno-tehničkih i psihosocijalnih aspekata zdravstvene zaštite pacijenata. Nedostatak edukacije o empatiji, naglasak na liječenju unutar trenutne akademske kulture, veliki broj pacijenata koje liječnici moraju podnijeti, kao i nedostatak adekvatnog vremena, svi su faktori koji negativno utječu na razvoj empatije.

1 Introduction:

Since I was young, I have always been fascinated by the concept of human connection. As time goes by, I started to wonder more and more regarding the question — what is the power that holds and connects people together in a relationship. After researching a bit and reading articles written by the best experts, I realized that the answer to my question was in front of me the whole time — the answer is Empathy.
Empathy is the foundation of any deep connection among people and it is the social glue that holds the society together. Empathy is the ability to see clearly into the nature of distress and still stay strong.

A Hassidic tale by Rabbi Shlomo of Karlin:
"If you want to pull a man from the mud, do not belive it will suffice to hold out your hand to him. You will have to sink into the mud next to him, so that you can hold him in your strong arms and bring him back with you into the light"13]

In the past people thought that empathy is something we were born with or without. Today we know that empathy can be learned with prctice, like most communication skills.

In this review I will share with you the fascinating journey I went through following the power of empathy and human connection.
Journey that begins in the distant past, contineues in the present and points into the future. We will define and understand what empathy actually is, we will compare empathy to other types of subjective emotions such as sympathy, and compassion. Furthermore, we will dive into the depths of the human brain in order to understand which parts of the brain takes place in the "Empathy circuit", how the brain processes emotions and mental states of the other as part of an experience of empathy. In this review we will explore and asses the role of Empathy in medicine and understand the importance of empathy in physician-patient relationship and how its impact is reflected in health outcomes.

2 Historical overview of the concept of Empathy

The concept of empathy has been widely described, discussed, and explored throughout history. Since antiquity, the importance of empathy for individual and collective good has captured the imagination of poets and scholars alike17].

The word 'Empathy' originally derives from the Ancient Greek terms *Empatheia* which means physical affection and passion, and *Pathos* which means passion or suffering. These terms were used by Aritstotle in his Rhetoric to describe strong emotion. In the late 19th century, the German psychologist Theodore Lipps (1851- 1914) translated the term *Empatheia* into the German word, *Einfuhlung* ("feeling into"), a state in which the perceiver loses self-awareness as his identity becomes fused with the object he is observing.28] In 1905, Sigmund Freud (1856-1939), a German psychologist that admired Lipps's work, developed the concept of *Einfuhlung* in order to explain the psychology of jokes and humor in his book 'Jokes and their Relation to the Unconscious'. Freund views 'Empathy' (Einfuhlung) as the conscious or unconscious process that allows us to understand others by putting ourselves in their place and believed that this is the only way to gain any opinion about the mental life of others.32] In 1909, the English psychologist Edward Titchener (1867-1927), translated the German word *Einfuhlung* and first introduced the word “Empathy” into the English language in order to describe the capacity of human beings to relate with another’s emotions and to know and understand one another through reflection and shared experience.27] 19] In the following decades, many psychologists extended the term 'Empathy' to the understanding of other people.

3 Empathy, Sympathy and Compassion

3.1 Definitions.

Empathy, sympathy, and compassion are three different terms that may be difficult to define and are often confused with each other.
All three terms represent subjective emotions that describe different levels of human interpersonal relationships by involving sharing of another person's emotional states especially feelings of distress or suffering.26]

3.1.1 Empathy

Empathy is the ability to emotionally understand other person's moods, mental states, and conditions and to feel what they feel from their perspective by putting ourselves in their shoes ("I feel how you feel").
Based on Becky Lynn Omdahl's explanations, empathy can be defined as the "capacity to think and feel oneself into the inner life of another person" and as "an affective response that stems from the apprehension and comprehension of another's emotional state or condition".10]
Empathy consists of three domains (affective, cognitive, and somatic).
Affective empathy refers to the emotional parts of sharing an emotional experience with the other that drives a person to respond with appropriate action to what someone else thinks or feels. Affective empathy begins with conversion modeling of what the other person is doing and experiencing.
The anterior temporal lobe is the part of the brain that becomes active when we are interpreting behaviors (e.g. facial expressions) and emotions of other people around us to make sense of them and to find out what it is they are feeling. Lack of affective empathy can be seen in sociopaths and psychopaths
Cognitive empathy refers to self-projection which is the ability to project our point of view in space and imagine what other things look like from different points of view. Self-projection allows us to understand how other people see the world (the thoughts, intentions, desires, feelings, or beliefs of another person). Lack of cognitive empathy refers to autism. *Somatic empathy* refers to 'Emotional Contagion' which is the tendency to automatically mimic/adjust facial expression, vocalization, body posture and movements of others.
Empathy occurs not only in negative situations where one person shares the

other's distress, but also in situations where we also understand positive emotions and manage to share with someone his joy.

3.1.2 Sympathy

The term 'Sympathy' is derived from Greek (*Sym-* which means "together with" and *Path-* that means “suffering” or “passion”)35] and has been conceptualized as the ability to feel the pain and suffering of others from our own self-oriented perspective without being able to exactly understand their pain ("I know how you feel"). Sympathy requires someone to understand another person’s feelings on an intellectual level. It is a shallow and superficial emotion that involves thoughtful words or gestures usually exhibited by individuals who wish to remain emotionally distant from another person's situation. This elicits an automatic, shallow, and pity-based reaction to a distressing situation that happened to another person expressed by giving unasked advice that can drives disconnection.

3.1.3 Compassion

The term 'Compassion' is derived from the Latin word *compassio* which means to "suffer with" and has been conceptualized as the ability to feel concerned and care for another person in response to their emotional distress and to feel strongly motivated to relief that distress by helping them**.**

3.2 Comparison

Empathy has components of sympathy and compassion, but it also carries relevant connotations that neither sympathy nor compassion has.26] Empathy and sympathy seem to refer mainly to the experience of the empathizer, while compassion seems to be more geared towards the target.11] Whereas empathy considers a passive action that doesn't provide a solution, sympathy and compassion consider active actions that come with unasked advice or with a solution respectively. From a Buddhist standpoint, sympathy is defined as an emotional reaction that occurs without conscious thinking and reflection. Empathy is a more complex interpersonal construct that involves awareness and intuition, while compassion considers a way to

develop the kindness ,support, and encouragement to promote the courage we need to take the actions we need in order to promote the flourishing and well-being of ourselves and others. Whereas sympathy was described as a self-motivated, emotional reaction to another person's suffering based on a lack of comprehension of the person’s needs, empathy was described as an affective response that acknowledges and seeks to understand an individual’s suffering through emotional resonance.35] In contrast to empathy where emotional resonance seemed to function as an endpoint, the emotional state of the listener in sympathy is emotional dissonance. In relation to compassion, emotional resonance was coupled with an intention to transform suffering, requiring the responder to move from “feeling with” (empathy) to “feeling for” the patient. Compassion, like empathy, fuels interpersonal connection through communication that focuses on listening without judgment, recognition of emotions and feelings (high sensitivity to non-verbal cues), and deep understanding. Secondary analysis of the data subset was conducted from larger grounded theory research which collected interview data from 53 advanced palliative cancer patients’ about their experiences, understandings, and preferences of the concepts of sympathy, empathy, and compassion in a clinical setting. In this study, patients reported that, unlike sympathy, which was described as an unwanted pity-based response that focuses more on alleviating the observer's distress toward patient suffering, empathy and compassion had a positive effect on their care experiences, allowing them to feel heard, understood, and validated. In addition to these patient outcomes, compassion was distinguished by its orientation toward action, its foundation in unconditional love, and its expression through small supererogatory acts.

	Sympathy	**Empathy**	**Compassion**

Type of action	Active action that comes with unasked advise	Passive action - doesn't provide a solution	Active action that comes with a solution
Type of response	Reactive responses evoked when something bad happens to another person	Skilled response	Reactive responses evoked when something bad happens to another person
Response to a distressing situation	Pity-based, unhelpful and misguided response	Emotional response	Action oriented and warm response (the listener is ready to help to relieve the suffering)
Communication	Listening with judgment + Giving un-asked advice	Listening without judgment	Listening without judgment
The listener emotional state	Emotional dissonance	Emotional resonance (putting ourselves in other's shoes) and emotional contagion	Emotional engagement and resilience
Interpersonal connection	Drives interpersonal disconnection	Fuels interpersonal connection	Fuels interpersonal connection

4 Neurobiological basis of Empathy:

4.1 Introduction

Emotions play an important evolutionary role and the development of certain areas of the brain is associated with the appearance of emotions in mammals. In order to understand the concept of "human emotions" and the mental states we experience in our life routine, we must first understand the biology and brain mechanisms behind these processes. Empathy has been passed on throughout the course of evolution and it is originally evolved to promote parental care for their offspring. When discussing evolution, it is important to first understand the two fundamental evolutionary forces that allow a certain gene or set of genes to be widespread in humans. The first evolutionary force, *Genetic drift*, is a random process by which certain genes disappear from a population over time due to random events such as war, natural disasters, etc. Genetic drift affects all genes equally and does not favor adaptive genes. The second evolutionary force, *Natural selection*, is a non-random process by which certain genes disappear from a population over time due to poor adaptation to the living conditions of the carriers. In order for a gene to be favored by natural selection it must give the individual an advantage in terms of reproduction and survival. For example, natural selection favored genes responsible for language skills and the ability to empathize because these abilities were important for our survival. The brain develops rapidly in the womb and continues at an accelerated rate in the first two to three years. Three major elements influence brain development. The first element, breastfeeding and parental care for offspring are related to the development of higher sensitivity to other people's emotions. The caregiver’s behavior is epigenetically transmitted to the child and affects the infant's lifelong health via later stress reactivity. There is also a link between skin contact and brain development. Tactile stimulation, such as rubbing the abdomen of caretakers and expecting mothers, promotes brain development. The second element is mother-offspring audio-vocal communication. The third element is play behavior. It mimics adult behavior, aids in the establishment of social rules, and thus profoundly changes the brain. The development of these three behaviors is related to the development of the thalamocingular component of the limbic system, which is linked to the prefrontal cortex by nerve pathways.

Parts of empathy first appear at an early age. In children as young as one and a half years old, there are early responses of empathy to someone else's distress. In adolescence, there is a progression of empathic abilities and in adulthood, the empathic abilities are more complex.25]

4.2 Deciphering the brain

Over the past two decades, various studies have used neuroimaging methods (e.g., functional MRI) to investigate which parts of the brain are activated when people empathize with someone else and to prove the hypothesis that our brain is "wired" for empathy. In these studies, the scientists used precisely timed experimental designs to elicit empathy in participants and fMRI to measure their blood-oxygen-level-dependent (BOLD) changes.
The designs enable scientists to compare BOLD responses during different subtypes of empathy and compare them to control conditions that do not require empathy. The findings of these studies revealed that we comprehend others' feelings and perspectives by utilizing and processing brain regions that are active both when we ourselves have a sensory, affective, or physical experience of suffering, and when someone else has a similar experience.
The ability to empathize with others is enabled by two different mechanisms. The first mechanism of empathy is through the 'Shared' brain networks (e.g., Mirror neuron system and Pain matrix), and the second mechanism is through the theory of the mind (ToM) or "Mentalization" brain networks.22] [24]

4.3 "Shared" brain networks theory:

Our brains work with shared neural circles. Activation of these neural circles has been linked to the genesis of empathy and it is in line with the hypothesis of shared brain networks. It has been proposed that when empathy is triggered by sensory stimuli such as seeing body parts in pain or hearing action sounds, the mirror neuron system, the pain matrix, and some core emotion-related brain regions such as the anterior cingulate cortex (ACC) and Anterior Insula (AI) are all triggered simultaneously.24]

4.3.1 The Mirror neuron system (MNS):

Mirror neurons are a special group of neurons that form a network of motor brain areas that respond similarly. It is composed of brain areas such as the inferior frontal gyrus, sensorimotor regions (i.e., rostral inferior parietal lobule), and posterior superior temporal sulcus. Many models of the MNS suggest that mirror neurons respond both to action observation and action execution. Whenever we perceive an action of another person, mirror neurons automatically translate this action onto our motor system as if we were performing the action ourselves. This mechanism allows us to predict another person's action as well as understand the intent and feelings underlying those actions. Mirror neurons were first discovered in macaque monkeys in the 1990s when a group of Italian scientists from the University of Parma noticed the same neuron responded not only when the monkey was performing an action (e.g., taking peanuts), but also when he was watching the researcher performing a similar action. This research helps neuroscientists find the basis for social interactions and it leads to new insights (how and why we develop empathy for other people), to more knowledge about autism, schizophrenia, and other brain diseases characterized by weak social interactions. Mirror neurons are the physiological and biological reason behind the term emotional contagion. Anatomical and neurophysiological data in the non-human primate brain and imaging human data suggest that the circuit of frontoparietal networks (composed of inferior frontal and posterior parietal neurons) interacts with the superior temporal cortex. During the execution and observation of an action, the frontoparietal circuit discharges, and the superior temporal neurons discharge only when an action is observed. Action representation and imitation rely on this interaction, and information processing in this circuit would flow as follows. i) Looking at someone else's facial expression encourages the appearance of a similar facial expression on our face, even when there is the unconscious recognition of stimuli. A key brain area involved in processing facial expressions is the superior temporal cortex which is a multisensory region showing sensitivity to non-verbal social signs including biological motion, actions, eye gaze, and vocalizations. The superior temporal cortex encodes an early visual description of an action and sends this information to posterior parietal mirror neurons (the robust anatomical connections between the superior temporal and posterior parietal

cortex facilitate this flow of information). ii) The kinesthetic information about movement is encoded by the posterior parietal cortex of the brain and is sent to mirror neurons in the inferior frontal gyrus, the rostral motor region. iii) The inferior frontal gyrus is involved in controlling facial movements that code the goal of the action linking to cognition. Cognitive processes enable the viewer to directly judge others' internal emotional states and to make explicit inferences about them. iv) Efferent copies of motor plans are transmitted back to the superior temporal cortex from the parietal and frontal mirror areas, allowing a matching mechanism to occur between the visual description of the observed action and the predicted sensory consequences of the planned imitative activity. (v) Imitation can begin once the visual description of the observed action and the sensory consequences of the planned imitative action match.14] The appearance of a similar facial expression in us stimulates changes in our autonomic nervous system, which contributes to the appearance of the appropriate feeling. The autonomic nervous system responds to stimuli from the environment that pose a threat to us or indicate safety with the most adaptive response (activates the sympathetic nervous system in fear, and the parasympathetic nervous system in relaxation) thus ensuring the survival of the individual.15] If, for example, we see someone laughing, our mirror neurons for a smile will also be activated creating a feeling in our mind that is associated with a smile. We will have such an experience immediately and without any effort.

4.3.2 The pain matrix:

Pain is a subjective experience stimulated by the activation of neural representations of current or potential tissue damage. These representations include somatic-sensory characteristics and affective-motivational reactions that stimulate behavioral responses with the aim of protection or recovery. Affective pain experience motivates behaviors aimed at interrupting, reducing, or avoiding exposure to a source of painful stimulation. Expressing pain can encourage other people to comfort or care for us important in the context of empathy. The pain matrix includes the anterior insula, anterior and middle cingulate gyrus, and primary and secondary somatosensory cortices.

Interestingly, the pain matrix, like the MNS, is active both when one experiencing pain and when one observes another person experiencing pain.

Perception of someone else's pain:

Research suggests that neural circuits are activated in one's own experience of pain and in the perception of other people's pain experiences partly overlap.

The anterior cingulated cortex (ACC) plays an important role in the motivational-affective dimension of pain. Listening to the crying of the newborn in the mother leads to increased activity in the ACC, anterior insula, medial thalamus and parts of the frontal cortex. In general, various studies using fMRI have shown that activation of the anterior insula, and dorsal ACC occurs during pain perception in other people. Some studies have examined whether there are differences in the activity of ACC and anterior insula in one's own suffering and in observing the suffering of others. It has been noticed that when observing other people's suffering, there is a greater connection between the medial prefrontal cortex and ACC, and the anterior insula. The prefrontal cortex is activated because we try to explain other people's mental and emotional states while suffering. In contrast, in one's own suffering, there is a greater association of some parts of the midbrain and periaqueductal gray matter (the part of the brain important for experiencing pain) with the anterior insula. Research conducted in 2004 by Singer suggests that brain areas such as the dorsal anterior cingulated cortex, cerebellum, and brainstem were activated when a person felt pain or watched another person experience pain. But only the actual experience of one's own pain led to the activation of the primary somatosensory cortex and the ventral regions of the ACC. For example, when observing the facial expressions of disgust of other people the part of the brain that is activated is the anterior insula. When observing painful facial expressions of other people the parts of the brain that are activated are the anterior cingulate cortex and anterior insula.

4.3.3 Theory of the mind (ToM):

Theory of mind (ToM) or “mentalization” network is thought to be the second route for empathy. It is thought to arise during conscious intention understanding of others, as well as during self-referential thought.
The “mentalizing network” and taking someone else's perspective involves imagining how the other person feels and what they are experiencing.
When we imagine ourselves in the place of another person in a situation that leads to some social emotions, the amygdala and parts of the temporal lobe are activated. Other brain regions have been demonstrated to be active when someone thinks about the mental states of another person.
When we try to relate to the way other people think, parts of the prefrontal cortex (medial prefrontal cortex, frontopolar cortex) and right temporoparietal junction (TPJ) are activated. The temporoparietal junction is an important region for self-awareness and recognizing the difference between self and others. Processing in this network enables sharing other’s states based on one’s previous experiences and knowledge. ToM can be divided into cognitive and affective processes. The cognitive aspect of ToM is necessary to understand what someone else may be thinking, his intentions, and beliefs while the affective aspect of ToM is necessary to understand how someone might feel given a specific situation. ToM may require both cognitive and affective components, however, specific brain areas may play more prominent roles in cognitive perception (ventral medial prefrontal cortex) or in affective perception (ventral medial frontal lobe).

4.4 Emotion-related brain regions

Affective empathy is thought to elicit emotion-related brain regions that are involved in the processing of feelings and emotions. 24] Emotional-related brain regions and affective empathy commonly include the limbic system (e.g., hypothalamus, hippocampus, amygdala, basal ganglia, anterior insula, and nucleus accumbens) that is responsible for processing emotions, the anterior and middle cingulated gyrus, as well as the ventral and medial parts of the prefrontal cortices. Activity in the anterior insula and amygdala are commonly known to be involved in affective processing and are thought to be related to affective aspects of empathy along with regions of the Mirror neuron system

(i.e., Inferior frontal gyrus). The amygdala is thought to be related to emotional learning that assists in the recognition of fearful facial expressions. By processing information from the viscera that arises when emotions occur, the anterior insula may be necessary for interpreting body states as affective feelings. When someone feels nervous ,this may be because his brain (anterior insula along with other brain areas such as regions of the brainstem) has noticed an increase in his heartbeat, clenching in his gut, sweat being produced, and has interpreted that change in body state as nervousness.

4.5 Regulation of empathic response

Emotional regulation means adjusting the balance between self and others. Empathy ends with fine-tuning the balance between self and others. Individuals with better emotional regulation are more likely to experience empathy and behave prosocially because they are usually able to inhibit their emotions for the good of others. The part of the brain that mediates this inhibitory mechanism is the medial prefrontal cortex. Whenever this brain area doesn't work well we will notice Narcissism. People whose emotions are more intense (especially negative ones) are more prone to personal anxiety when looking at other people's negative emotions, which prevents prosocial behavior. The experience of empathy and personal anxiety can be influenced by socio-cognitive factors. Interpersonal factors such as the closeness or similarity of the observer and the person suffering affect the occurrence of empathy - we empathize more with more similar and closer people. People that have to inflict pain on others in their work (e.g., health care workers), when observing other people's suffering, there is less activity of parts of the brain involved in the perception of pain - they are inhibiting their emotions for the good of others.

4.6 Hormones and empathy

The hypothalamus-pituitary-adrenal (HPA) axis is involved in the neuroendocrine regulation of empathy via the secretion of three key hormones oxytocin, testosterone, and cortisol.37]

4.6.1 Oxytocin

Oxytocin is a neuropeptide hormone that is synthesized in the hypothalamus by the paraventricular (PVN) and supraoptic nuclei (SON) and travels along axonal projections to their terminals in the posterior pole of the pituitary gland where they are released into the bloodstream in response to signals from their hypothalamic cell bodies. Oxytocin acts as a neurotransmitter and a hormone with central (amygdala, hippocampus, and brain stem) and peripheral (heart, womb, and spinal cord) effects. It suppresses the activity of the hypothalamic-pituitary-adrenal axis (active in stress response) and that elicits a relaxing effect. 34] Oxytocin affects the central nuclei of the amygdala, thus inhibiting the effects of reduced emotional empathy and aggressive behavior affected by testosterone. Oxytocin is crucial to our ability to modulate empathy. It is important for establishing attachment between humans (e.g., partners, a mother with her child, etc), it encourages positive social behavior and a sense of trust in other people and it increases the ability to recognize other people's emotional states based on subtle signs. 3]

4.6.2 Testosterone and Cortisol and the Dual hormone hypothesis:

Generally, women tend to outperform men in tasks requiring emotional and cognitive empathy and tend to self-report higher dispositional empathy than men. On the other hand, men are more likely than women to suffer from social cognition disorders such as autism spectrum disorders [2] [37] and psychopathy (disorders that are characterized by a lack of empathy). Since men, on average, have much higher testosterone than women, it is possible that testosterone is inversely related to empathy. As a result, it is believed that sex differences in empathy are accounted for, at least in part, by gender differences in testosterone. In terms of mechanisms, by affecting the activity of the amygdala, testosterone can reduce emotional empathy. The hypothesis that empathy is negatively associated with testosterone is the key assumption behind the "extreme male brain" theory of autism, which suggests that ASD is characterized by deficits in cognitive and emotional empathy due to the organizational effects of fetal testosterone.

In addition to testosterone, the hypothalamus-pituitary-adrenal (HPA) axis may also be involved in the neuroendocrine regulation of empathy. The HPA

axis plays an important role in the stress response by releasing glucocorticoids (e.g., cortisol), which fuel the organism with the energy required to face a stressful situation. Although few studies have specifically, mostly indirectly, investigated the effects of cortisol on empathy, it has been suggested that the expression of emotional empathy may correlate with high basal cortisol concentrations as well as with stress-induced cortisol increase. Testosterone and cortisol may influence empathy separately, or jointly. The activities of the HPA and the hypothalamus-pituitary gonadal (HPG) axes, which lead to the secretion of cortisol and testosterone respectively, are intrinsically co-regulated. Specifically, cortisol can inhibit the secretion of testosterone at all the levels of the HPG axis, while testosterone can act upon the hypothalamus to inhibit cortisol release. An imbalance between cortisol and testosterone in the direction of high baseline levels of testosterone and low baseline levels of cortisol is correlated with features of psychopathy. Based on these studies of testosterone and empathy, it could be hypothesized that high testosterone and low cortisol should be associated with lower empathy. This idea would also be congruent with the dual-hormone hypothesis, according to which physiological and behavioral aspects of dominance and aggression should be more pronounced in individuals with high baseline testosterone and low baseline cortisol levels.

5 Empathy in medicine

In medicine, empathy refers to the ability to understand the personal experience of patients without bonding with them. It is considered a crucial ingredient in personal development and is essential for the full range of social interactions. Being empathic is a very complex, demanding, and strong (but gentle) way of being. Personal distress can arise in us due to someone else's emotional state which can be very intense and disturbing, causing us an aversive reaction (e.g. anxiety, worry, anger), which can then prevent us from helping others.

5.1 Doctor-patient relationship and the role of empathy:

The ability to care is an important aspect of social life and feeling concern for other people implies empathy. Empathy is a vital communication skill for health workers, and it serves as one of the fundamental tools for the development, enhancement, and improvement of the therapeutic relationship between doctors and their patients. It is widely acknowledged that physician empathetic ability leads to better diagnosing and planning procedures, more successful patient treatment, and to better health outcomes. To efficiently establish a therapeutic relationship with patients, doctors use effective medical interviewing that combines the traditional therapist-centered interviewing with patient-centered interviewing which focuses on the personal and emotional aspects and encourages the patient to spontaneously describe his or her symptoms. This medical interviewing allows the interviewer to obtain a more complete story about the patients' lives, considering the combination of biological, psychological, social, and spiritual factors .Additionally, it enables the physician to recognize and understand the patients' inner experiences, concerns, and perspectives so that he can comprehend their needs and help them express the thoughts and problems that concern them. As a result, the distance between the doctor and his patient reduces, enabling both to enjoy mutual benefits. Empathetic relationships that develop between doctors and patients over the course of treatment reinforce the cooperation towards designing a therapeutic plan and a personalized tailor-made intervention, enhancing therapeutic effects because patients better adhere to the therapeutic course of action, increasing

the patient's satisfaction with the therapeutic process. In this way, health care quality is improved, the number of errors is diminished, and the percentage of health care recipients who positively experience therapy is increased. 29]Although the importance of empathy is undeniable, a significantly high percentage of health professionals seem to find it difficult to adopt a model of empathetic communication in their everyday practice

5.2 Neurobiological bases of doctor-patient relationship:

According to Fabrizio Benedetti 6] the process of the doctor-patient encounter can be subdivided into four behavioral and biological steps:
The *first* step - "Feeling sick" is a crucial starting point that involves the sensory systems that convey different pieces of information related to peripheral organs, as well as brain regions that lead to conscious awareness. (e.g., pain can be the product of Bottom-up processes taking place in the peripheral and central nervous system and of top-down processes taking place in the cognitive and emotional brain areas. The *second* step occurs when a person seeks help to suppress discomfort by activating motivational mechanisms and brain reward mechanisms. These two steps are critical in leading the patient to look for a doctor who himself represents a powerful reward. The *third* step is when the patient meets the doctor.
A special and unique social interaction occurs in which the doctor represents the means to suppress the patients' discomfort. Here many intricate mechanisms are at work, such as trust and hope on the one hand and empathy and compassion on the other. These complex functions take place both in the brain of a sick person, where expectations, beliefs, trust, and hope play a central role and in the doctor's brain, in which empathic and compassionate behavior represents an essential factor.
Finally, the *fourth* step is when the patient “receives the therapy”.
A mere ritual of any therapeutic act (effective or ineffective) and the therapeutic doctor-patient relationship may generate therapeutic responses through the patient's expectations and beliefs (placebo or nocebo responses), which are sometimes as effective as actual medical treatments.

5.3 Are medical students being trained to treat patients empathetically?

Most students begin training with a high capacity for empathic engagement with patients, but this capacity erodes as they progress through their clinical training. A cross-sectional study was conducted during the academic year 2017/2018 to examine variation in empathy scores (JSE) in a national sample of 10,751 medical students in different years (1st – 4th) and clinical phases of medical school. The researchers used a web-based survey to collect information about the students' demographic factors (e.g., age, gender, race or, ethnicity), medical school education year, areas of specialization, plan to pursue a subspecialty, healthcare employment prior to medical school, and undergraduate major. The study findings revealed statistically significant differences in mean empathy scores by year of medical school. The researchers noticed a significant decline in JSE mean score, especially during the clinical phase (third year) compared with the preclinical phase of medical education. 23] Reasons for this erosion of empathy include a lack of formal empathy training, stress, emphasis on emotional detachment and clinical neutrality, over-reliance on technology that limits human interactions, inadequate/lack of mentoring, and inappropriate treatment of medical students.33]

6 Special situations in medicine

6.1 Empathy in working with patients with PTSD:

Post-traumatic stress disorder (PTSD) is a mental and behavioral health disorder that can develop after witnessing or experiencing a very stressful, frightening, distressing, or traumatic event that may involve a real or perceived threat of injury or even death. Traumatic events such as natural disasters like an earthquake, military combat, physical or sexual assault, an accident, or chronic disease such as cancer, cause structural changes in the brain (e.g. Hippocampus that is twice lower size than usual) which leads to alterations in the natural fight-or-flight response, causing the people that suffer from it to feel stressed or fearful, even when they're in a safe situation.31]

This sense of serious current threat has two sources: the nature of the trauma memory (which leads to intrusions of the trauma and other re-experiencing symptoms) and excessively negative appraisals of the trauma and/or its sequelae.36] They tend to shut themselves in, and have difficulties believing in people due to the fear of being harmed again. As a result, they avoid making social connections and do not integrate into society.

Empathy is a complex phenomenon that has an important role in the therapeutic process with psychotraumatized patients. For such a patient to open up and share his emotions, a strong relationship based on trust is required between the therapist and patient. Listening without judgment to trauma stories and the ability to remain sensitive and finely attuned to the internal experience of the individuals' psychological injuries requires more than understanding that an event was traumatic. It requires skills and a biological and psychological capacity to use empathy to access the inner scars of the psyche and the organism itself.9]

6.2 Empathy in working with patients in palliative care:

Palliative care defined as specialized complete care provided for patients in the final and irreversible stage of progressive or terminal chronic diseases, for patients suffering from severe irreversible brain damage, and for patients

whose illness is no longer responds to treatment such as patients with metastatic cancer (70%) and patients suffering from other chronic diseases (e.g. MS, ALS, Alzheimer's disease, CVI, severe heart failure, COPD or fibrosis). Palliative care seeks to alleviate burdensome symptoms and stress that accompany serious illness, including debilitating pain associated with chronic illness and the dying process. It considers both the patient and the family as the primary focus of care to improve their quality of life and includes the period of grief. 1] 33] Empathy is a key quality for palliative care teams that include doctors, nurses, and social workers who collaborate with a patient's other clinicians to provide an extra layer of support. Empathy as care model is a medical intervention characterized by a tendency to treat the patient as a person through a strong sense of care, executed through empathy. Competent and effective palliative care means not only skilled practice in the science and techniques of pain and symptom control, but also in the art of creating and maintaining relationships, as well as the use of oneself as a primary diagnostic and therapeutic instrument. 37] The palliative team is a confident companion to the patient in his or her inner world. Members of the team lay aside their own views and values in order to enter the patient's world without prejudice. Working with patients in palliative care requires being sensitive to the changing felt meanings that flow in this other person, to fear and anxiety, rage, tenderness, or confusion they might experience without judgment and in a vulnerable manner without trying to uncover unconscious feelings since this would be too threatening or scary. It includes sharing the palliative care provider's sensing of the person's world as he looks with fresh and un-frightened eyes at elements of which the patient is fearful as well as frequently checking with the person as to the accuracy of the sensing, and being guided by the responses he receives. Perspective-taking is a cognitive empathetic capacity that assists palliative care providers in better understanding how another person thinks about their emotions and, as a result, helps them to communicate with patients and their families clearly because the provider can put the information across in a way that will make it easy for them to take in. While explaining things to a patient, it is essential to ensure that the patient fully understands everything.30]

"Communication portrays as a strengthening factor for patient care and families as it strengthens them to have hope and motivation to fight the disease" 20]

In research reports on 53 palliative cancer patients' experiences of sympathy, empathy, and compassion in the palliative care unit the patients described empathy as a more emotionally engaged process. This is because the providers of care attempted to attune to the patient's emotions through acknowledgment of suffering. Patients perceived this as a warm, gentle attempt to understand their emotional state.35]

7 Empathy and society

7.1 Empathy, culture, and trans-national concepts of empathy:

Empathy is based on social interactions and is defined as the understanding, awareness of, sensitivity to, and ability to vicariously experience the feelings, thoughts, and experiences of another.5] Empathy is positively related to subjective well-being and life satisfaction, emotional intelligence, and self-esteem. Compared to less empathetic people, empathic individuals have larger and more fulfilling social networks, and they are more pro-social (for more altruistic reasons they volunteer more, donate more to charity, and are more likely to help others in need).6] Culture plays a critical role in shaping how and when people respond to others' suffering with empathy.17] It socializes us to relate to other people in different ways, potentially affecting how empathy is experienced and expressed. In the study "Differences in Empathic Concern and Perspective Taking Across 63 Countries",18] the researchers examine cross-cultural variation in empathy, explore cultural variation in empathy, and explain how this variation is related to psychological characteristics, emotional expression and experiences and prosocial behavior across cultures. To conduct the study the researchers used data provided by other cross-cultural studies to situate their sample [104,365 adults (61.2% men), ranging in age from 18-90 years, across 63 countries with the majority residing within the United States] within a broader nomological network of psychological characteristics and prosocial behaviors operationalized as charitable donations, volunteerism, and helping behavior. The researchers found that whereas parents from individualistic cultures (e.g. Western parents) generally focus on teaching children the benefits of being independent and unique, parents from collectivistic cultures (e.g. East Asia) stress the strong interconnection of individuals. They teach their children to fear loneliness and isolation and due to that, they show more negative reactions to separation from their caregivers compared with children from individualistic cultures. Thus, the thoughts and feelings of people in collectivistic cultures may be more closely tied to the thoughts and feelings of others around them, which may account for their higher level of trait empathy compared with people in more individualistic cultures. Countries with higher levels of empathy also had

higher levels of collectivism, agreeableness, conscientiousness, self-esteem, emotionality, subjective well-being and life satisfaction, and prosocial behavior.

7.2 Empathy in the time of technology:

For years we have all lived - Technology. Pursue it and get excited about it. Live in a culture of perfectionism and hyper-individualism. We have always felt that technology serves us, gives us a better and fuller life, that technology has come to meet human needs and expand our capacity, using resources (knowledge, materials, and money), tools (systems and devices), and processes (design and manufacturing). Most people think that technology is neutral, that it simply exists as an object, and that we choose to use it whenever we want. In recent years something has changed - technology is taking over us, drawing our attention and dictating our opinions and agendas. Is it possible to turn the wheel back? Probably Not . . .
20-30 years ago people used regular phones to communicate, watched TV, and listened to the radio. Today, on the other hand, from the moment we wake up to the moment we fall asleep, from the bathroom to the line at the coffee shop, our heads are always on these devices. We not only use these devices, but we also live by them. We have created technology that has a lot of advantages but it also destroys us. Technology involves impacts on society and the environment. In the last era, we are experiencing a sharp increase in the use of technology and as a result, we are witnessing a change in the way people interact and spend their time. Everyday communication is conducted mostly via online channels through screens instead of in person. Empathy is like a muscle that needs to be developed and nurtured and it develops through communication that is done in person face to face. In order to develop empathy, a child needs to experience the situation of standing in front of a friend and insulting him in order to see his facial expression, expressing hurt and insult - this is how he learns to recognize sadness.

7.3 Empathy and the media:

As with anything related to humans, media in general and social media, in particular, cause us an intriguing combination of fear and enjoyment.
We enjoy watching TV, keeping up to date on Facebook about what is happening in the world, getting interesting posts on WhatsApp, and following our friends on Instagram. On the other hand, the time we spend on social media arouses our fears of lack of control. All over the world, people feel that something bad is happening on social media. They have cracked the "human operating system"- They have cracked us. The social media learn about us very quickly, how our brain works, and discover our weaknesses, then succeed in predicting how we will behave and how to influence us. Social media shapes our life perceptions, it injects lies and hatred in a way that endangers us and it inevitably has a toxic effect in that it increases the feeling of loneliness, depression, anger, self-hatred, eating disorders, and bullying. Social media affect not only us but also our relationships with our spouses and the people closest to us and by that they win in every aspect of our lives. People behind the scenes become crueler and crueler and many of them (especially children) are dragged into abusive conversations and bullying on social media without even knowing who the victim is.

Conclusion:

Empathy is person-centered not condition-focused and every person has the right to be seen, understood, and appreciated. The human capacity to automatically comprehend and connect with others, termed empathy, is an intangible gift and real human connection in healthcare and society is important more than ever. While it may be assumed that healthcare workers are naturally compassionate and empathetic, unfortunately it’s not always the case. Developing empathetic skills should not only be the underlying objective in the teaching process of health care undergraduate students, but also the subject of the lifelong and continuous education of professionals.

Empathy extends far beyond a patient’s medical history, signs, and symptoms. It goes beyond clinical diagnosis and treatment. Empathy encompasses a wide range of emotional experiences and psychological concepts. It is also encompasses a strong connection and a deep understanding of the patient's mind, body, and soul. It is a very effective and strong tool for gaining patient trust, reducing anxiety, and improving health outcomes.

Nevertheless, it seems clear from this review that cultivating empathic concern or compassion in today's medicine is more important than other aspects of empathy, like vicariously experiencing and introspecting about patients' emotions. Specific neurobiological mechanisms explain the benefit to patients of their physicians’ perceived empathy.

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