Title: EPIGENETIC IMPRINT OF "COMPASSIONATE SOCIETY" TRIGGERED BY VULNERABILITY AND MENTAL ILLNESSES

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Summary:
Epigenetics investigates the connection between our genes and our environment. It has been hypothesized that certain conditions we experience can influence our gene expression and can probably be passed onto our children, transgenerational transfer of trauma being one of them. We postulate that the notion of compassion has also been passed on from one generation to another. Our ancestors discovered that groups have a higher chance of survival than individuals. Thus, psychological traits that help form social cohesion, like compassion, are proven beneficial and passed onto the next generation.

However, our perception of compassion has changed through time. In the beginning, it was expressed as a feeling of sympathy for the vulnerable, for example the elderly, the sick, pregnant women and children. These groups were innately perceived as deserving compassion. As our social awareness grew, so did the list of vulnerable groups, including members of different races, sexual or gender orientations, etc. Over time, a shift in the way we feel compassion has occurred.

Nowadays, it almost seems like only those belonging to a vulnerable group are justified to feel suffering or oppression. At the same time, the suffering of those who do not belong to these exclusive vulnerable groups is marginalized. Mental illnesses like anxiety or depression are trivialized if the person in question is perceived as being privileged (in any sense), while at the same time, they are seen as warning signs if the person suffering is vulnerable. If one truly needs attention, help, or both, the easiest way is to declare oneself vulnerable. If this trend continues, we postulate that a lack of compassion in our modern society will have an impact on future societies as well. Through transgenerational epigenetic inheritance, this can create future societies whose sense of compassion will be shaped only by the definition/perception of those who are currently perceived as vulnerable.

Key words: compassion - epigenetics - mental illness - society - vulnerability

Introduction:
“Empathy” and “compassion” are two words that are often used interchangeably, but they are not synonymous with one another. Empathy is defined as the ability to perceive and understand the emotional experience of others. To put it simply, empathy means that one feels what the other person feels. Compared to empathy, compassion is a broader term. It does not pertain to sharing the emotional experiences of others; it is an emotion itself. Compassion appears when one witnesses the suffering of another, and it serves as motivation for providing help to those in need. We are motivated by the suffering of others and wish to help, regardless of them being close to us or being complete strangers. Compassionate individuals want to support, understand and help vulnerable ones (Goetz et al. 2010). Compassion is innate; however, it can be influenced by numerous social factors that can either suppress or enhance it (Lown 2015).

Compassion is, for example, of great importance in the healthcare system. Ill people are especially vulnerable, and they want to be treated with care and compassion (Perez-Bret 2016). Treating patients with compassion results in better clinical outcomes: patients are happier with healthcare service, and quality of communication between doctors and patients is improved (Strauss et al. 2016). Research also shows that compassionate treatment of patients can reduce postoperative pain (Egbert et al. 2013), decrease hospitalization rates for diabetics (Canale et al. 2012) and even increase survival chance of patients suffering from cancer (Dahlin et al. 2010).

However, can we say that this is enough? That society is compassionate on all its levels if health professionals have incorporated it in their everyday work? That by being sick, in pain and distress, with a diagnosis that correlates with poor outcome, one can truly expect compassion and to be treated in a compassionate way, no matter what our social, racial, or other background may be? To expect fair and compassionate treatment not only from doctors, the healthcare system, but from the surrounding society as well? And what about health conditions, which are not supported against? For example – mental illnesses?

Lack of empathy in population can prove to be especially troublesome for those suffering from mental illnesses. Studies conducted around the globe have shown that those issues are not limited by geographical position, nor culture (Lauber & Rossler 2007, Abdullah & Brown 2011, Stith 2011). Stigmatization...
of mental illnesses and discrimination that arises from it are both topics of scientific inquiries (Semrau et al. 2015).

Some studies focused on evaluating the extent of discrimination towards people suffering from mental health issues and whether there is a difference between high-income countries (HICs) and low- and middle-income countries (LAMICs) (Chung & Wong 2004; Koschorke et al. 2014). Surprisingly, research showed that LAMICs had lower rates of discrimination when compared to HICs. As stated in the study of Semrau et al. (2015), a discrepancy was observed in both common, e.g., major depression (Oshodi et al. 2014, Lasalvia et al. 2015) and severe mental disorder, e.g., schizophrenia (Thornicroft et al. 2009, Koschorke et al. 2014).

Those findings seem to align with earlier research concerning stigmatization which suggested that the stigma of mental illnesses was present in nonindustrialized societies to a lesser degree. Proposed explanation is that those societies provided a more supportive environment, emphasizing the importance of social cohesion and community, as opposed to the more traditional western sense of individualism, therefore lessening the risk of feelings like rejection, isolation, segregation and institutionalization (Littlewood 1998).

**BIOLOGICAL AND EVOLUTIONARY BACKGROUND**

Compassion has always been strongly related to human offspring. Human offspring are very dependent on care provided by their family and society, especially at an early age. A common saying, often ascribed to the African continent, says: “It takes a village to raise a child.”. It is considered that compassion developed during human evolution is an effective element of caregiving system. Compassion enabled vulnerable offspring to reach the age of viability in which procreation of species is possible (Gilbert 2015, Goetz et al. 2010). Throughout history, people who were willing and able to help have been perceived as more desirable partners, both in mating and non-mating relationships, because they provide mutualistic benefits (Barclay 2016).

The first societies of our ancestors from the Pleistocene were like communities of other social primates. Important neuropsychological changes have happened in the past two million years, and they have enabled bigger and more cooperative societies, which are key features of modern human species. Unlike other social primates, whose cooperativity is mostly limited to kin, humans also cooperate with other non-relatives, and even with different species, because of benefits on physiological processes and social relationships (Gilbert 2015, Boyd & Richerson 2009).

Humans are the only species that has established caregiving system for the ill, which developed as a unique set of cognitive and sociocultural specializations. This system was a successful mechanism of disease control in social communities, even when they grew bigger. Although the system stopped disease spread, it increased the risk of spreading socially transmitted disease. This made evolution of pathogens easier, which prompted evolution of the human immune system. After hominines separated from the rest of the primate order, brain size and the capacity for social learning increased. The system in which offspring are taken care of by other members of society (besides their parents) is considered key for psychological changes like the ability to understand others’ mental states, empathy and hypercooperativity. It is thought that these cognitive traits are most important for recognition of illnesses, which is a crucial element of social and cognitive features, connected with an increase of social complexity in Homo genus (Kessler et al. 2018).

It is of utmost importance that offspring are taught knowledge and skills by their elders during childhood. This increases survival and fertility rate (Garay et al. 2018). In conclusion, the care system leads an increase in human lifespan.

**EPIGENETIC IMPRINT AND COMPASSIONATE SOCIETY**

Epigenetics investigates how our environment influences our genes. It has been hypothesized that certain conditions we experience, such as trans-generational transfer of trauma (Kellermann 2013), can influence our gene expression and probably be passed onto our children. We postulate that compassion has also been passed on from one generation to another. Our ancestors discovered that individuals are less likely to survive than groups. This proves that psychological traits, which help form social cohesion, like compassion, are beneficial and passed onto the next generation.

The neurohormone oxytocin is considered crucial for evolution of the neocortex, which is responsible for complex social interactions and social bonds. Oxytocin has an important role in regulating social interactions. It is especially important in forming attachments and social behaviours. It also increases social sensitivity during life. Humans who are more sensitive to others’ feelings and emotions will be more prone to show positive social behaviours (Kumsta et al. 2013, Carter 2014), such as compassion.

The question is: can changes in compassion that happen under influence of social factors somehow be passed onto the next generation, and if yes, how? Epigenetics, science that studies all potentially stable changes in gene expression that occur in the absence of changes to the DNA sequence, can give us the answer to this question. Epigenetic mechanisms
can explain the link between environmental influence and permanent changes in physiology and behaviour.

One of the best studied epigenetic factors, that influence gene expression, is DNA methylation (Kumsta et al. 2013). The methyl group (\(-\text{CH}_3\)) bonds covalently to 5-C atom of the cytosine ring with DNA methyltransferase (DNMT) enzyme, where 5-methyl-cytosine (5mC) is made (Ziller et al. 2013). This reaction is reversible, which means that methyl groups in the genome can be removed by enzymes in the process of demethylation (Ramchandani et al. 1999).

Cytosines (C), which are a part of CpG dinucleotide, are most often methylated in mammals. Most of CpG dinucleotide is methylated (70-80%), while the rest of unmethylated CpG is organised in dense clusters, so called CpG islands. CpG islands are often found in promotor gene regions and they are connected to active gene expression (Kumsta et al. 2013, Ziller et al. 2013). DNA methylation, as a stable and easily measured epigenetic marker, is often at the centre of epigenetic research in epidemiology and neuro-psychiatry (Kumsta et al. 2013; Guintivano & Kaminsky 2014).

The oxytocin receptor gene (OXTR gene) is considered to be crucial in finding the answer to the question of passing compassion to the next generation. There is an evidence that the gene, which codes for the oxytocin receptor (OXTR), can be epigenetically modified by experiences. OXTR methylation is connected to differential activation of brain regions involved in social perception. For example, exposure to psycho-social stress can dynamically regulate methylation of OXTR gene (Kumsta et al. 2013).

Epigenetic information was considered unpassable to offspring until recently, because of reprogramming events, like global DNA methylation followed by histone modification reprogramming, which happened during gametogenesis and after fertilisation. However, changes in DNA methylation in previous generation can be passed on to the next one, because there is a large number of genes linked to methylation regions, which are resistant to erasure during gametogenesis (Guintivano & Kaminsky 2014, Tang et al. 2015).

Intergenerational transmission is direct transmission of epigenetic traits from parents to offspring, because the factor which causes epigenetic change can affect the exposed and its sex cells at the same time. Here we refer to transgenerational inheritance where the epigenetic change of interest is expressed in the first non-exposed generation. In men, that is F2 generation (grandchildren), and in women, that is F3 generation (great-grandchildren) (Skinner 2008).

Even though the aetiology of mental illnesses is unknown, it is hypothesized that mental illnesses are a result of genetic predisposition and negative influence of environmental factors, which influence the genome through epigenetic modification. The environmental risk factors for developing mental health disorders are connected to specific developmental time periods where their effects can be most influential. If there is environmental exposure during these periods, epigenetic changes that reprogram key genes can happen, increasing the risk for mental illness. Over time these changes may culminate in a disorder, mediated by epigenetic mechanisms (Guintivano & Kaminsky 2014).

But many of those epigenetic changes still need a trigger which can be environmental, social, cultural, emotional, physiological. No matter which trigger is combined with genetic predisposition and/or epigenetic processes they will all happen in the context of the specific society surrounding the organism in question. Society will create nuances between “acceptable” and “unacceptable” conditions. Humans are mostly motivated by self-interest, but at the same time they are social beings (Cropanzano et al. 2005). We humans have a history of violence within our own species, but despite this, we still need social interactions in everyday life. Without social interactions, humans cannot evolve, or even survive (Carter 2014).

Society itself is never considered as being health determinant, it is always perceived as being socio-economic or socioenvironmental determinant.

Socioeconomic status (SEP) is a fundamental determinant of health. People with higher socioeconomic status have more material resources that allow them better access to available healthcare, while people with lower socioeconomic status are more exposed to a larger number of stressful events, which lead to poorer health. There is preliminary evidence that SEP is a regulator between methylation and risk of PTSD in genes primarily related to nervous system function (Uddin et al. 2013).

In studies that used the classical twin design, relatively large ranges of heritability and environmental influences have been identified for many mental illnesses. Illnesses that showed relatively high levels of inherited risk were schizophrenia, bipolar disorder, Alzheimer’s disease, autism, attention deficit hyperactivity disorder (ADHD) and panic disorder. On the other hand, major depressive disorder (MDD), anxiety, somatiform disorders, and alcohol abuse showed lower heritability according to twin studies. Genome-wide significant results in MDD suggest that mental illnesses with low heritability may be more under control of environmental influences. For example, environmental factors which increased risk for MDD development are sexual abuse, hormonal fluctuation and stress. Schizophrenia is linked to prenatal risk factors, including mother malnourishment and infection (Guintivano & Kaminsky 2014).
DISCUSSION

Perceiving socioeconomic and socioenvironmental influences on mental illnesses as a base for transgenerational epigenetic impact on individuals should also be seen as part of a wider concept of imprinting the sense of vulnerability into society. If the society is desensitized to suffering, except to those who claim to be underprivileged, future generations will, grow up with a skewed view of vulnerability. In regards to this we postulate that this will give rise to a general lack of compassion as well. The proposed mechanism would happen on two fronts: first one is social level – learning by example in a social environment that neither recognizes nor responds to the suffering of the not enough visible vulnerable individuals. The second is epigenetic level - by depriving individuals of experiencing empathy and compassion at a neurochemical level and passing on those imprints onto the next generation.

This is an ongoing process, exemplified by the results of current anti-stigmatization campaigns concerning mental health. As Semaru et al. (2015) have concluded in their research, current anti-stigma campaigns have been flawed. Although they managed to educate the population in viewing mental health issues as being predominantly based on biology, somewhat equalizing them with other somatic issues, they failed in lessening the perceived discrimination of mental health patients.

We hypothesize that one of potential causes for that discrimination is current growing lack of empathy in Western society. With the rise of individualism and growing emphasis on personal responsibility, it is often easy for society to judge those who suffer from mental health issues, often attributing their illness to internal factors, i.e., laziness or entitlement. This is in line with previous studies which showed that Western societies worsen the prognosis of psychiatric patients by emphasizing their personal responsibility in the illness they face (Littelwood 1998). It seems that if there is no “properly” visible vulnerability, there will not be a compassionate response from society.

Yet, members of “self-declared” vulnerable groups receive more sympathy, as their status implies that their suffering is not caused by internal factors, i.e., lack of personal responsibility, lesser degree caused by lack in personal responsibility, but rather that the origin of their suffering is to be attributed to external factors, such as oppression, discrimination and traumatic events. This turns the attribute of vulnerability into a marker of justified suffering.

However, our perception of compassion has changed throughout time. In the beginning, it was expressed as a feeling of sympathy for the vulnerable, such as the elderly, the sick, pregnant women, and children. These groups were innately perceived as the ones who deserve deserving compassion (Charli Carpenter 2005). As our social awareness grew, the list of vulnerable groups grew as well, including members of different races, sexual or gender orientations, etc (Nifosi Sutton 2017). Still, we witness numerous situations where stress related disorders, as a consequence of different power distribution in some professions (“empowerment through empathy”) attract more attention and society’s compassion than mental illness. Over time, obviously, a shift in the way we feel compassion has occurred.

What is the problem then? That we do not see the vulnerability where it is needed to be seen or that we are compassionate only when vulnerability is publicly presented? “For all those women working night shifts in hospitals or stocking things in grocery stores or working in many industries where there is more anonymity and not the same levels of public scrutiny or, in many cases, fame, it must be pretty frustrating to feel that your complaints are not being taken with similar seriousness,” said Ann Marie Lipinski, curator of the Nieman Foundation for Journalism at Harvard (Pazzanese & Walsh 2017). And she is right, the more one is publicly visible (and/or famous) the more their voice can be heard. Is this enough? Will this effect “spill over” to other situations as well? Mental illnesses for example? Or do we need a more complex approach?

We believe that if we miss the opportunity to teach our societies to be compassionate about mental illness, we will transfer this attitude to the next generation and the stigma will persist. This will happen simply because our attention will not be focused on the very nature of illness an individual is struggling against. Rather, the focus will shift from the illness onto self-promoted health conditions or currently socially acceptable vulnerable positions pertaining to socio-economic status, race, gender etc. We need compassion to be incorporated in our societies that will teach our descendants to spot vulnerability (without self-declaration) and provide assistance where it is needed, regardless of our biases towards other groups. Those characteristics need to be imprinted in our genes, providing social cohesion and strength for future evolutionary leaps.

CONCLUSION

Nowadays it almost seems like only those belonging to a vulnerable group are justified to feel suffering or oppression. At the same time, the suffering of those who do not belong to these exclusive vulnerable groups is marginalized. Mental illnesses like anxiety or depression are trivialized if the person in question is perceived as being privileged (in any sense), while at the same time they are seen as warning signs if the person suffering is from a perceived vulnerable popu-
lation. If one truly needs attention, help, or both, the easiest way is to declare oneself a member of a vulnerable group. If this trend continues, we postulate that a lack of compassion in our modern society will have an impact on future generations. Through transgenerational epigenetic inheritance, this can create future societies whose sense of compassion will be shaped only by the definition/perception of those who are currently perceived as vulnerable.

Mental illnesses need stronger public presentation while modern societies are prone to be sensitive to well-promoted health conditions in relation to vulnerability of those suffering from the aforementioned conditions. Compassion shown to people with mental illnesses is important for our survival while our evolutionary history teaches us that empathy and compassion differentiate our development from all other species. Epigenetic imprint occurs throughout our lives and can be transferred to our descendants, while modern societies are prone to be sensitive to vulnerability of those suffering from the aforementioned conditions. Compassion shown to people with mental illnesses is important for our survival while our evolutionary history teaches us that empathy and compassion differentiate our development from all other species. Epigenetic imprint occurs throughout our lives and can be transferred to our descendants, and a more compassionate approach to vulnerability can be a strong trigger which drives us to strive to be better and to reach our full potential.

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