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The role of epigenetics in post-covid adaptation

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Abstract

For a long time, we have been used to think of the connection between the studies of psychopathology and molecular genetics in terms of "predictive factors." The development of Psychoneuroendocrinoimmunology (PNEI) represented an important change that prompted us to redefine the theoretical assumption under which genetics and the environment, in their interaction, determine the construction of the human being.

In this epistemological framework it has become possible to introduce a new field that continues to revolutionize all branches of medicine: epigenetics, understood as neural plasticity, the ability of the brain to be modified, both during development and as an adult, by experience and from the environment. Psychotherapy therefore proposes itself as a meeting ground with other medical sciences and begins to consider epigenetic change as the fulcrum of its effectiveness.

As regards the epigenetic impact of childhood trauma, there is growing evidence that epigenetic variations can be observed among individuals who have experienced adversity in childhood.

The plasticity of DNA methylation and post-translational modifications of histones, in response to both postnatal and adult life experiences, suggest that epigenetic mechanisms may have evolved to allow organisms to adapt to changing environmental conditions.

Pychotherapy's role, becomes of primary importance in an era in which it is necessary to deal with the consequences of a long period of stress due to the health emergency, what we can define "post-covid adaptation". Overcoming this challenge can have a significant impact on the brain's ability to react resiliently and pass this skill on to subsequent generations.

In fact, the strong stress experienced can have short and long-term effects on the way of coping, and epigenetics is therefore at the center of the reflection of the researcher who wants to take up the challenge of finding new intervention tools to develop resilience methods, such as new life approach.

Introduction

Epigenetics can be defined as the way in which the environment interacts with the genome at the molecular level. It is a transversal discipline that also has a lot to say in the field of the study of the psyche: it can be considered the "bridge" (together with neuroscience) capable of connecting biology with psychotherapy, because it demonstrates that the environment does not interact with DNA exclusively through evolution, but can do so directly through interaction with the individual through the action of mechanisms that modulate gene expression. Psychotherapy, the discipline that integrates the contributions of Psychology and Psychiatry, has always embraced an organicist western tradition and, in the course of its evolution, has considered the individual psychological characteristics in the most homogeneous and linear way possible, to the point of suggesting the construction of theoretical assumptions such as temperament, personality or character, with the specific intent of creating theoretical models useful for "drawing" the evidence observed. Meanwhile, the development of knowledge relating to brain plasticity is increasingly orienting studies towards a more neurobiological psychotherapy perspective, which reflects the dynamic nature of the interaction between genes and the environment [1]. This epistemological framework arises from the integration of the contributions of genetic psychiatry and neuroscience and psychotherapy. Epigenetics is therefore a transversal discipline that, probably, in the future will open new ways of studying and considering things in respect of the study of the psyche as well as in that of mental health [2].

In fact, we are witnessing the emergence of a completely new social landscape, hopefully definable "post-covid". In fact, during the period of the health emergency, the disruption of normal forms of social interaction have taken place, with a consequent devastating effect on the psyche of adults and even more of children and teenagers. The "traditionally" contexts, like schools, forms of sporting aggregation, groups of friends, disappeared. Children / teenagers saw themselves inserted into these contexts through a screen, almost as if they did not experience everything in first person. And even when the first reopenings took place, it happened under the banner of fear, of distancing, almost as if the "other" was no longer a point of reference for knowing each other, like a friend, but like a potential enemy, bearer of death.

In case of more traumatic situations, such as those in which a loved one passed away, the experience was made even more painful by the impossibility of resorting to the usual social farewell rites, which allow one to 'adapt', within the limits of the possible, to the sad experience of loss, and to give the last farewell to the loved ones.

Epigenetics and mental health

If the environment has the power to intervene in such an important way, it is ethical to ask ourselves until what point we should be

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confronted with the repercussions that the traumatic period collectively experienced, due to the changes in the pandemic, will become evident. And again, what are the procedural measures and methods in the psychotherapeutic field to be adopted and monitored. The studies of the nineties by Kandel [3] have long been guiding the developments in neuroscience which confirm the efficacy of psychotherapeutic treatments. The modifications intervene not directly on the DNA sequence (for example on the succession of bases that make up a gene) but on its structure [4].

What we are has not already been written and contained in our genome, but, as amply demonstrated, it is determined by a process of dynamic interaction between the genome and our environment. The experiences made in the everyday environment would, in fact, be able to model the activity of genes, through the so-called epigenetic modifications, and therefore the relationships between genotype, phenotype and environment would be governed by similar molecular processes. Human's experiences are encoded within our DNA through particular and precise gene regulation mechanisms, which come into play already during embryonic development [5]. Epigenetics is a branch of study that deals with changes that affect the phenotype without altering the genotype. It consists of a series of molecular pathways through which the transcription is altered, without however modifying the underlying DNA sequence (transcription is the process by which the information contained in the DNA is transcribed by enzymatic way into a complementary RNA molecule). Exposures to the environment that affect genes are varied and concern the type and level of nutrients taken during development, the toxins to which one is exposed and the level of stress both in infancy and in the stages of subsequent development. In addition, animal studies have shown how the effects of social experience affect the epigenetic pathways that influence characteristics such as the response to stress, learning, memory and reproductive behavior [6].

The influence of environment

Epigenetic mechanisms give a high degree of plasticity and stability to the gene expression pattern of each individual, however it was thought that the flexibility of these mechanisms (in particular methylation) in response to signals from the environment was limited to the early stages of embryonic development.

Instead, it has been widely demonstrated that individual differences in gene expression can arise in the face of individual environmental experiences that occur throughout the life span, not limited, then, to the first contacts with the external environment during childhood [7].

In humans, studies on monozygotic twins have provided interesting results regarding the potential of epigenetic plasticity to drive divergences at the phenotype level.

In these studies, [8,9] methylation and acetylation patterns were highly concordant among twins under 28 years of age, but diverged significantly between older twins (over 28 years), leading to speculation that this divergence emerges in response to unique experiences of each twin. Therefore, epigenetic changes not only take place in the early stages of development, but also during adult life, as a response to adaptation to the external environment. The influences of the social environment can also contribute, during development, to build certain epigenetic patterns.

Decades of longitudinal and laboratory studies [3,10] highlighted the association between the quality of the social environment and the neurobiological and behavioral consequences on animals and humans. In particular, some of these studies [11] have focused on the quantity of mother-child interaction and its correlation with the type of social competitive encounters that are established in adulthood.

As regards the epigenetic impact of childhood trauma, there is growing evidence that epigenetic variations can be observed among individuals who have experienced adversity in childhood [12].

The plasticity of DNA methylation and post-translational modifications of histones, in response to both postnatal and adult life experiences, suggest that epigenetic mechanisms may have evolved to allow organisms to adapt to changing environmental conditions.

Highly stressful events (bereavement, abuse, illness, trauma) leave their mark both in the body and in the psyche, especially on a child or a teenager.

The period of emergency due to the pandemic can undoubtedly be classified as highly stressful, both because of the losses in terms of human lives it entailed, and in terms of social relations, of the reassuring 'normality' [13].

As for the loss of affection due to be reavement, it was further aggravated by not having had the traditional tools for processing it, in terms of social farewell rites, such as funerals [14].

Even for adolescents, suddenly finding themselves without the normal reference institutions such as school, group of friends and sport, this resulted in a particularly difficult situation. For a long time they have been found themselves confined behind a screen, like "seeing themselves" talking, studying, playing, a difficult situation for everyone but in particular for individuals of the adolescent age group, characterized by the search for their own identity.

The effects of traumas can also be inherited and manifests in descendants, in the form of physical or psychological health problems, psychiatric pathologies and developmental disorders.

This was demonstrated by a study [6], conducted by a research group of the Tufts University School of Medicine in Massachusetts and published in Translational Psychiatry, which confirms how traits of frailty in children can be linked to epigenetic alterations transmitted to them by their parents.

What is inherited is not a DNA sequence associated with the trauma, but a variation of how genes express themselves - thus manifest themselves - in the phenotype.

The researchers analyzed, in a group of human volunteers (28 adult men), the relationship between a past trauma and the possible presence of such epigenetic modifications.

The researchers offered the volunteers the Adverse Childhood Experiences (Ace) questionnaire, a 10-question test that is used to detect trauma during childhood and adolescence: among the most stressful events, physical or psychological abuse, neglect, lack of care, parental divorce etc.

After identifying the traumas, they proceeded to identify the microRNAs (also present in human sperm) as some evidence has shown that external factors, such as smoking and obesity, can alter them. But only today we have the proof that stress can impact these components.

The results showed that the trauma is linked to the levels of two miRNAs detected in human spermatozoa, called miR-449 and miR-34.

Volunteers who had experienced particularly severe and protracted traumatic events had 300 times lower levels of these two miRNAs than those who had suffered minor trauma.

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In addition, with previous experiments on mice, [6] researchers had shown that these variations were associated with anxiety and problems in the sociability of guinea pigs for at least three generations.

These studies confirm that epigenetic changes are stable and heritable and that stress is therefore also heritable. It would be important to take epigenetic modifications into account also to get a clearer picture of a patient's physical and mental health.

Epigenetics: the relationship with psychotherapy and neuroscience

The psychiatry interest in epigenetics began with the research on the epigenetic mechanisms that influence the normal patterns of neurodevelopment of brain functions and, consequently, of the mechanisms that intervene in the inadequate development implicated in some psychiatric disorders [10].

Subsequently it was considered that the epigenetic modifications that occurred during uterine life have an influence on adult life, however, the influence of environmental factors can influence epigenetic "remodeling". These factors include drugs, chemicals, but also psychosocial aspect [8].

Meanwhile, the development of knowledge relating to brain plasticity is increasingly orienting studies towards a more neurobiological psychotherapy perspective, which reflects the dynamic nature of the interaction between genes and the environment [1]. Neural plasticity is the ability of the brain to be modified, both during development and as an adult, by experience and the environment [9].

These changes are reversible (unlike the genetic ones that alter DNA sequences) so, theoretically, one day one might be able to intervene to restore low miRNA levels in men exposed to extreme trauma.

In this epistemological framework, which arises from the integration of the contributions of genetic psychiatry and neuroscience, psychotherapy, in addition to being capable of causing real changes in the morphology of the brain, truly deserves the definition of "epigenetic drug" provided by Stahl [8] because it may be capable of bringing about a biological change that is reflected in human thought, behavior, interaction.

Epigenetics can over time provide instructions and encouragement for the promotion of mental health through an approach capable of going "beyond" well-defined trajectories [14].

To be clear: embracing the well-known model of Cloninger [14] the probabilities that a young novelty seeking will develop ADHD or a personality disorder of cluster B of the DSM do not depend on the genetic passivity predisposed by temperament but depend on environmental factors capable of epigenetic modifications. Prevention should therefore aim at the creation of adequate and personalized psychosocial environments, capable of giving space to psychotherapeutic interventions that can involve the systems (family, school and professional) in which people interact and live at various levels. it is negatively correlated with a deteriorated mental state, which is why the study results could be used to implement social support measures aimed precisely at the population groups that seem to emerge as the most affected [15].

Conclusion

It is easy to understand the importance of dealing with a biopsycho-social perspective also with how the current socio-economic situation resulting from the Covid-19 pandemic impacts from an epigenetic point of view in terms of mental health. The public debate that has arisen in many countries following the prolonged lockdown is also called to address the difficult compromise between health and the economy. If many suffer from the loss of their loved ones (loss of life), many more will suffer from their own chance to survive (loss of livelihood). The issue is rather complex, also because the side effects of the lockdown, including the economic and mental health consequences, are less easy to identify than epidemiological issues, such as the number of infections and deaths caused by Covid-19. Consequently, and also partly because of this complexity, some issues have received less attention both in the public opinion and in the scientific research.

The necessity to deal with a long period of stress due to the health economy, instead, gives psychotherapy a role of primary importance. Overcoming this challenge, from an epigenetic point of view, can have a significant impact on the brain's ability to react resiliently and pass this skill on to subsequent generations.

A situation of strong stress can have short and long-term effects on the way of coping, and epigenetics is therefore at the center of the reflection of the researcher who wants to take up the challenge of finding new intervention tools to develop resilience methods, such as new life approach.

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