ECRONICON OPEN ACCESS

EC PSYCHOLOGY AND PSYCHIATRY
Review Article

Epigenetics and Genetics Weave the Thread of Self

Frédérique Perrot Tafforeau*

Doctor in Cell Biology, Society of Psychosomatics Intensive, Rue Abbé Philippe Le Gall, France

***Corresponding Author:** Frédérique Perrot Tafforeau, Doctor in Cell Biology, Society of Psychosomatics Intensive, Rue Abbé Philippe Le Gall, France.

Received: May 22, 2019**; Published:** June 25, 2019

Abstract

The human being is made by its experiences and all of its memories, as cellular as cerebral, past as present, are building its future. The biology allows us to bring the well-established scientific proof.

To do so, as soon as the conception is made, its environment influences the construction of the individual during the embryogenesis thanks to the epigenetic process.

Then, the different critical periods of the development give a brain maximal plasticity window facing the "different learning process".

Finally, during adulthood, once all of these periods are over, the synaptic plasticity works so that individuals have access to a certain adaptability. However, the critical periods of the development reopening researches during adulthood leaves us supposing that a meeting, a therapy, a strongly lived event, be quite capable of reopening this plasticity adequately substantial to remove the individual life's trajectory.

Keywords: *Embryogenesis; Epigenetic; Critical Period of Development; Influence of the Environment; Brain Plasticity; Adaptability; Homeostasis*

Phyllogenetics tells us that the first organisms such as bacteria did not have a nervous system. The latter tend to cluster together, surrounded by a gangue polymer that they synthesize to form bacterial biofilms. A biofilm could be compared to a tissue within which each cell communicates with the neighbor via molecular signals that, by modifying the environment, will induce a new physiological response of the neighboring cell receptor. If the signal is reiterated, this physiological change will be memorized by processes called epigenetic mechanisms.

These epigenetic phenomena maintain a homeostatic balance and correspond to an adaptive mechanism. There is a cellular memory that precedes the establishment of a brain memory.

How is an organism built?

Like bacterial biofilms, embryogenesis, with its cellular diversification, is underpinned by epigenetic processes, which will continue to work for life for an adaptive purpose.

We thus speak of silent embryogenesis, taking up a Bernardian concept (Claude BERNARD 1813-1878) "life is death, life is creation". Constantly and ad vitam, the system dies, and is recreated in a physiological homeostatic equilibrium, due to a process of permanent regeneration. When this physiological process "derails", it leads to pathological.

At the beginning of life, the construction part is more intense than the destruction part, then the dynamic is reversed, the destruction part takes precedence over the construction part. In the adult this phenomenon of regeneration is silent.

Regeneration is a construction not only as growth, but also as a morphogenetic process. If our cells are replaced, we remain in spite of everything ourselves. After 10 years, we do not have a single cell of origin, however we remain recognizable. The form is maintained. The process is organo-morpho-genic.

The human is the result of all his past and present memories (cellular and cerebral), all of which builds his future...

Epigenetics and embryogenesis. Basic intuits

The newborn is built from a single cell, a unique genetic heritage.

Each of its cells contains the same genetic information, inherited from the mother cell whose multiplication has generated a hundred different cell types. Each cell type has its specific properties, and must keep in mind its function, age, and position in the body.

Data is added to the information provided by the genes. This allows the diversification of genetic potentialities within different types of cells and is stably transmitted during cell generations to constitute functional organs and tissues during development according to the organomorphogenic process.

Epigenetic control tells which genes in which organ and when they should be active. This is the second code of our genome.

First, DNA (Deoxyribonucleic acid) determines the genetic code and secondly epigenetics regulates gene expression. The term "epigenetic" means beyond, beside genes; it is a code that acts "over" the genetic code (Greek: ἐpí epi: adverb: above, preposition: on)

Genes and the environment are interconnected through epigenetics.

Epigenetics is a normal process during development. It allows the diversification of potential readings of genetic information and produces cell differentiation. Epigenetics fills the gap between the innate and the acquired, between robustness and plasticity, between the solid and the flexible, the established and the random.

Epigenetic mechanisms: Molecular basis and definitions

The cell has a special structure: the nucleus that includes the genetic heritage called DNA, chromosomes or genome.

Genetics is the study of hereditary traits that are transmitted according to Mendel's laws.

Genetics refers to the writing of genes, and epigenetics refers to their reading.

The same gene can be read differently depending on the circumstances. The sequence of nucleotides (DNA) that make up these genes is not changed. In contrast, the proteins encoded by these genes may be produced at different times or places depending on the epigenetic marks that are present and act on the genes. These marks result from the environment of a gene.

Epigenetics corresponds to stable, hereditary, and reversible change (this trait is specific to epigenetics) of a gene in the absence of a change in the DNA sequence.

The identity of a cell is the result of a balanced marriage between genetics and epigenetics. Genetics thus constitutes, predisposition, the innate characters, and the epigenetics will record during the development the factors of adaptation.

Epigenetic strategies can be at different levels:

- At the DNA level,
- At the transcription level,
- At the level of translation...

The most studied are the methylation of the DNA, and the modifications at the level of the histones.

It is a combination between these different brands that will indicate whether certain genes or alleles must be "on" or "off" in certain cell types or at certain times. The same gene in a cell type is going to be in an "off state", with very particular marks that are associated, like methylated DNA, and particular histone markings, which gives a compacted chromatin: the gene will only be not expressed. In another cell type, the same gene may have different modifications that will lead to a rather open state, and the relaxed chromatin will allow the expression of this gene. These mechanisms of methylation of DNA and histones and acetylation of histones give the cells a certain epigenetic state that will contribute to the cellular identity.

Epigenetic modifications act in response to a decision of the cell, programmed by developmental signals.

It's a stable answer.

Epigenetics retains the memory of a cellular decision despite the disappearance of the inductive signal.

Epigenetics presents an inheritance

During cell divisions there is a clonal amplification, a decision that was made at a time t.

Epigenetics acts as an archive of cellular memory of development. This process is the basis of the constitution of tissues or homogeneous organs. During development it will allow to give phenotypes, traits, normal characteristics.

The reverse of this stability and this heritability begins when the signal is wrong. Wrong information will be archived and a pathological or aberrant cellular identity will unfold.

In response to developmental signals, the cells engage in a particular destiny, where transcription factors will be able, depending on the degree of compaction of the DNA, and via the processes of methylation, to activate or extinguish certain genes: the epigenetic brands will come to consolidate and perpetuate these decisions.

These changes are heritable during mitosis and/or meiosis, and do not result from modifications of the DNA sequence.

Positional information

The progress of each of these steps can be disturbed by the environment.

Stress, toxins and pollutants, diet, body effects induced by perilous situations can, among other things, disrupt the progress of each of these steps.

The iterative abnormal signals will induce responses that will be epigenetically consolidated constituting "lines of vulnerability", or even appearance of abnormal and pathological phenotypes.

In the development of the nervous system, positional information will play a central role.

The nervous system can be represented as a plate, a leaf on which a grid is drawn. This sheet closed in tube remains squared with dorso-ventral orientation and anteroposterior orientation. For each of these orientations, we note a concentration gradient of certain molecules called morphogens, which are, for the most part, transcription factors. These morphogens are molecules that allow the cell to engage in this or that differentiation path depending on their concentration. These are "signal molecules".

Positional information means that when the neural tube has closed and differentiated, a cell in a given region will give rise to a specific type of congeners, specific, for example, of the cortex. At the moment when the neural plate is formed, the cells are similar.

When the neural networks are built, the neurons send out an axon to another region to form a synapse, a neuronal contact. Navigation of the "cone of growth", the research head of the neuron, must be precise. The cone of growth is able to find a target sometimes very far in the three-dimensional space of the nervous system.

The grid of positional information is therefore fundamental to the construction of a functional nervous system as well as to the building of the individual.

The heterogeneity of the nervous system is limited, if we stick to the expression of neuromediators. The complexification of the cell population is linked to the expression of other factors, in particular these signal molecules (essentially transcription factors).

Thus, two dopaminergic neurons will not have the same molecular signature depending on their location.

For any cell type, there are two essential information related to the positional information: it is as if the cell had to ask two questions:

- Who am I: Am I an astrocyst, a neuron, a fibroblast, a muscle cell?
- Where am I: Am I a fibroblast of lung or foot? Am I a neuron of the cerebellum, cortex, or dark substance?

These two questions related to the position of the cell in the body, is a fundamental factor of its physiology.

The environment, by disturbing the normal developmental signals or by itself providing an aberrant signal, is able to induce accidents in the construction of an individual that may have effects on its physiology, by the effect of cascades. The homeostatic functioning of an individual involves a close interaction of all the systems (psyche, genetic and epigenetic, nervous system, immune system, endocrine system).

Modified positional information can lead to changes in brain cell populations (poor positioning of the edges), a change in nerve cell migration, poor axon guidance, altered cell proliferation ... and in turn, altered neural circuits causing cognitive changes and how to be in the world.

Any event during pregnancy (annoyance, influenza...) is likely to have an effect on the expression of these molecules inducing the expression of other genes

Positional alteration can occur at any level of regulation in a harmless manner. A catastrophic overshoot may result from the accumulation of errors during each of the physiological stages of these signaling systems.

Developmental aspect

A deleterious influence of the environment on cells can be expected to be most harmful when it occurs very early in development.

Are concerned:

- Reproductive cells, particularly sensitive, because they are the ones who carry all the genetic capital.
- The very early embryo is particularly vulnerable because it consists of only a few cells, and if there is a disruptive event capable of modifying the epigenome, amplified throughout the body.
- Some adult cells that divide very strongly that can propagate an epigenetic anomaly. This is the case of adult stem cells.

The influence of environmental signals will also be crucial during active methylation phases of the genome.

Thus, two main periods when the genome acquires a lot of DNA methylation correspond to extremely vulnerable phases: in gametes (oocytes and spermatozoa) and in the embryo (about twelve days old) which has just become established within the maternal uterus.

The periods of active neurogenesis, which correspond to the setting up of the CNS (central nervous system), will also be periods of extreme vulnerability.

The human is the fruit of his experience

In vertebrates, strategies of development, while defining a constraining plan, leave a great freedom to the details of the cerebral construction of which important aspects of the structure are modified throughout the existence. In man, it is the very history of individuals that fits into the cerebral structure through an uninterrupted process of individuation.

Brain condition undergoes permanent and major changes from a functional and structural point of view. The complicated architecture of the adult brain is the terminal product of genetic instructions, cellular interactions and exchanges between the child in development and the outside world. (the human exists only through the Other and is built only in relation to the Other...).

Brain development

Brain plasticity does not result exclusively from the effect of external events. Many internal events in a person's body, including the effects of hormones, lesions, and abnormal genes, also have effects on plasticity.

In its early development, the brain is particularly vulnerable to these internal factors that will in turn affect how the brain reacts to interactions with the external environment.

The early development of the nervous system is dominated by "environment-dependent" events, prior to the formation of synapses, which are, therefore, independent of any nervous activity. These include the establishment of the primordial nervous system during the early stages of embryogenesis (placement of positional information, initial formation of neurons from undifferentiated cells (or neurogenesis), migration from their production site to their final location). All the stages of the development of the nervous system, "environment-dependent" constitute so many "delicate" periods. This development is very robust, as has already been pointed out, but it is also very plastic and therefore able to respond to changes in the environment while being sufficiently buffered to remain within an acceptable homeostatic range.

These processes pave the way for the subsequent formation of specific axon paths, and the development of a multitude of synapses providing connections.

Synaptogenesis is one of the main steps in ontogeny of the human cortex. During the first waves of synaptogenesis, the cellular and molecular mechanisms and the consequences they have on development, since they make it possible to construct a nervous system of anatomical complexity that is difficult to imagine, are enough to create surprisingly advanced innate or automatic behaviors.

Thus, human newborns have innate abilities to learn, to categorize the objects of the world and potentially to symbolize. The fetus is even able to distinguish the maternal voice from other voices before birth.

During the last months of gestation, the growth of synaptic networks becomes influenced by the activity of peripheral sensory receptors (environmental representations) and proprioceptive (body representation). Thus, at the end of intrauterine development, and after birth, the intensification and survival of neuronal connections become dependent on sensory, emotional, and experiential inputs.

Man is a neotenic being, that is to say that its construction remains uncompleted at birth. The phases of the prenatal period until the end of puberty include critical periods of development of neuronosynaptic networks. These critical periods of development correspond to windows of maximal plasticity of the brain. During these critical periods, normal interactions with the surrounding and socio-cultural environment are necessary for the proper maturation of these circuits.

After adolescence, the environment can still modify synaptic circuits, but only locally.

Critical periods of development

Once brain connectivity is broadly defined, nerve activity profiles (including those triggered by the experiment) alter the synaptic cabling of the developing brain. Nervous activity resulting from interactions with the outside world during postnatal (and perhaps prenatal) life provides a mechanism by which the environment influences the structure, physiology and functions of the brain.

The nervous system of complex animals adapts to the particular conditions of its environment and is influenced by them. The concept of brain plasticity, or neuroplasticity, refers to changes that affect the structure of the brain. They take place throughout life and are based on lived experiences.

A critical period of development is defined as the moment during which a given behavior manifests a particular sensitivity to specific environmental influences that it requires to develop normally. Lack of exposure to appropriate stimuli during the critical period is difficult or sometimes impossible to compensate later.

When this period is over, the behavior is no longer significantly affected by subsequent experience (or lack of adequate experience). In fact, by completing its maturation, the human brain, like that of other mammals, becomes more and more refractory to the lessons of experience, just as the cellular mechanisms through which changes in connectivity are made become less effective.

Examples of critical periods of development

This example concerns the critical period for somatosensory representations (corresponding to the representation of the body and the sensoriality) and the constructions of our sensory homunculi. This representation is fixed approximately at 7 days after birth in the mouse. This critical period (which corresponds to the setting up of what Damasio calls somatic markers) is crucial in early mother-child relationships and one can imagine that the experience will allow the child to distinguish between the inner and the outside, him and not him, to access the perception of his own body, to distinguish emotions and sensations.

Reintroduction of plasticity in adults

Reducing GABAergic inhibition in adults helps reopen a period of plasticity in adults. Reducing the transmission of other neuromediators may also help close or reopen a period of plasticity.

For example, reducing cholinergic transmission in adults reduces plasticity. Similarly, administration of a benzodiazepine, a molecule that stimulates GABAergic receptors, reduces plasticity. Treatment with fluoxetine, a reuptake inhibitor of serotonin and norepinephrine, increases the extracellular concentration of these neuromediators, resulting in the temporary reopening of some plasticity in adults. This last effect is countered by diazepam, a benzodiazepine that mimics an inhibitory effect.

This is the adverse effect of the joint use of anxiolytics and antidepressants in the medical treatment of depressive states.

One can thus suppose that an astonishment, a romantic encounter, an event lived intensely, traumatically, will reopen a critical period of development in the adult and have a restorative or inversely deleterious effect [1-19].

Summary

The human is the fruit of his experience and all of his memories, cellular as well as cerebral, past and present, build his future. Biology allows us to provide sound scientific evidence.

Thus, from conception, the environment influences the construction of the individual during embryogenesis through epigenetic processes.

Then, the different critical periods of development offer a window of maximum plasticity of the brain in the face of "different learning".

Finally, in adulthood, once all these periods are over, synaptic plasticity works to allow individuals a certain adaptability. However, studies to reopen critical periods of development in adults suggest that a meeting, a therapy, an event lived intensely, be able to come reopen plasticity large enough to change the life course of the individual.

Conclusion

Individuality and individuality are built through all the interactions between the human being and his environment (in the global sense of the term) and this, from its conception, or even already during its prehistory.

During the intrauterine life, the maternal experience, by modifying the environment of the embryo, then of the fetus, contributes to shape the individual for a large part of its singularity.

Then, from birth, the mother-child interactions, and their affective quality will be of the greatest importance for the future of the individual. These interactions, but also all others, whether family, social, cultural, ecological, ... will shape the being and build it, as regards its relationship to the other, its food preferences, as its identity sexual, sexual preferences...

Thus, cellular memory, brain memory and environment interact throughout the life of the individual to confer its singularity, but also to change, to evolve.

Note 1

Example of the positioning of the edge between the mesencephalon and the metencephalon.

Both compartments are regulated by two transcription factors:

- The mesencephalon is regulated by the factor otx2
- The metencephalon is regulated by the factor gbx2.

On either side of this edge, there are niches that allow the development of subtypes of neurons determining in the development of pathologies of the nervous system.

In particular:

- A dopaminergic niche
- A serotoninergic niche.

These neurons innervate all parts of the cortex and are strongly involved in the regulation of mood.

O2 or gbx2 gene deletion experiments were conducted in mice.

Changes in the expression of one or the other of these genes cause a displacement of the edge, resulting in a larger niche for dopaminergic neurons or for serotonergic neurons. Thus, we obtain very important effects on quite viable animals. If the expression of otx2 is reduced, the mesencephalon and the dopaminergic niche are reduced. In the adult animal, there is a decrease in the secretion of dopamine and an increase in the secretion of serotonin. All this leads to behavioral effects. Notably, the deleted animals have a much more violent drug response than the control animals. In the opposite example, when the expression of gbx2 (increase in dopaminergic niche and decrease in serotonergic niche) is reduced, the adult mouse, which has too many dopaminergic neurons and not enough serotoninergic neurons, will be agitated, little secure. If an anti depressant is administered to this mouse, such as a serotonin reuptake inhibitor, it returns to a so-called normal state.

These data from animal models should be considered with great caution and cannot be extrapolated directly to humans. However, they show the importance of edge positioning and the impact of fluctuations.

It thus seems important to mention, in connection with the above, the fact that, in babies born to depressive mothers during pregnancy, the biology of dopaminergic and serotonergic neurotransmitters is that observed in depression.

Note 2

Another example is the critical period for language. Human individuals, need a prolonged post-natal experience to produce and decode the sounds that are the basis of language. It is important to note that the linguistic experience must, in order to be effective, take place at the beginning of life. The need to hear and practice language during a critical period is evident in studies of language acquisition by children with congenital deafness. While most babies begin to emit babbling-like sounds around the age of 7 months, deaf children have obvious deficits of early vocalization; these children will not be able to acquire the language if they are not provided with a mode of symbolic expression in another form. But if, very early (from about 6 months), these deaf children are exposed to sign language, they

begin to babble with their hands in the same way that hearing children babble orally. This suggests that there is a modeling of verbal behavior by early experience, independent of the modality. Children who have learned the language, but later become deaf before puberty, also exhibit a substantial decline in spoken language, probably because they cannot hear themselves and thus lose any opportunity. to improve their speech by auditory feedback during the last days of the critical period for language.

Certain pathological situations in which normal children have never been exposed to an appreciable amount of language show the same thing.

By elaborating a little more, it may be said that the phonetic structure of language that an individual hears in the first years of his life shapes both his perception and his production of speech. During the first months of life, infants can perceive and discriminate all the sounds of human language: they have no innate predisposition for the phonemes characteristic of this or that language. But this ability to distinguish the totality of phonemes does not last. By the age of 6 months, babies show a preference for the phonemes of their mother tongue and, at the end of their first year, they no longer respond systematically to the phonetic elements of other languages. The ability to perceive these phonetic contrasts, however, persists for several more years, as shown by the fact that children can learn to speak fluently a second language without grammatical errors and without accent until around 7 to 8 years of age. Beyond this age, performance gradually decreases regardless of the intensity of exposure to the language or its practice.

Some changes that occur in the developing brain are likely to explain these observations.

Studies comparing patterns of brain activity in 7 - 10 year olds and adults in very specific word analysis tasks suggest that for the same task, the same regions of the brain are not the same. activated in children and adults. The significance of these differences is unclear: they may reflect anatomical plasticity accompanying critical periods or different ways of performing language tasks in children and adults; however, they are an indication that brain circuits change to fit language during early childhood.

Although the phenomena observed with regard to language or other behaviors peculiar to the human species are examples of the most striking critical periods, it is difficult if not impossible to study in man the cerebral modifications of the mechanisms which underlie them. tend. The discovery of the physiological plasticity of the CNS, which has deepened our knowledge of the changes that occur in nervous wiring during critical periods, came from a series of considerable experiments in the early 1960s. conducted by David Hubel and Torsten Wiesel as part of their research into the development of the visual system in animals with high visual abilities (binocular vision) and particularly in cats and monkeys.

Note 3

Molecular aspect of the critical period of development.

All the factors that open the critical period and among which we will notably find trophic factors for survival and neuronal growth such as brain derived neuronal growth factor (BDNF), numerous posttranscriptional modifications of messenger RNAs, adhesion molecules, or still the morphogen, transcription factor OTX2, ... increase the maturation of the inhibitory circuits.

To prevent this maturation, makes lose the opening of the critical period.

Moreover, any treatment or accident that will increase earlier than expected cortical inhibition will open early the critical period, which is not always good.

Similarly, one of the etiology tracks of schizophrenia targets the late critical periods of development, at the edge of adult life for certain regions engaged in post-pubertal cognitive, social behavior. In fact, a hypothesis which is sufficiently widespread today, rests on the idea that it is in the bad course of these critical periods that the origin of psychiatric disorders appearing towards the end of puberty could be found.

Bibliography

1. Akbarian S. "Epigenetics of schizophrenia". *Current Topics in Behavioral Neurosciences* 4 (2010): 611-628.

2. Aravin AA., *et al*. "A piRNA pathway primed by individual transposons is linked to de novo DNA methylation in mice". *Molecular Cell* 31.6 (2008): 785-799.

3. Archer T., *et al*. "Epigenetics in developmental disorder: ADHD and endophenotypes". *Journal of Genetic Syndromes and Gene Therapy* 2.104 (2011): 1000104.

4. Bale TL., *et al*. "Early life programming and neurodevelopmental disorders". *Biological Psychiatry* 68.4 (2010): 314-319.

5. Benes FM., *et al*. "Regulation of the GABA cell phenotype in hippocampus of schizophrenics and bipolars". *Proceedings of the National Academy of Sciences of the United States of America* 104.24 (2007): 10164-10169.

6. Boulanger LM and Shatz CJ. "Immune signalling in neural development, synaptic plasticity and disease". *Nature Reviews Neuroscience* 5.7 (2004): 521-531.

7. Caviness VS., *et al*. "Numbers, time and neocortical neurogenesis: a general developmental and evolutionary model". *Trends in Neurosciences* 18.9 (1995): 379-388.

8. Deverman BE and Patterson PH. "Cytokines and CNS development". *Neuron* 64 (2009): 61-78.

9. Damasio A. "L'erreur de Descartes". Paris: Odile Jacob (1994).

10. Damasio A. "Spinoza avait raison. Joie et tristesse, le cerveau des émotions". Paris: Odile Jacob (2003).

11. Damasio A. "L'autre moi-même. Les nouvelles cartes du cerveau, de la conscience et des émotions". Paris: Odile Jacob (2010).

12. Damasio A. "Le sentiment même de soi, corps émotions, conscience". Paris: Odile Jacob (1999).

13. Mark J Millan. "Epigenetic framework for neurodevelopmental disorders: From pathogenesis to potential therapy". *Neuropharmacology* 68 (2013): 2-82.

14. Northoff G., *et al*. "Self-referential processing in our brain-a meta-analysis of imaging studies on the self". *Neuroimage* 31.1 (2006): 440-457.

15. Purves Augustine., *et al*. "Neurosciences". 3rd édition. Bruxelle: De Boeck Universités (2005).

16. Patterson D. "Genetic mechanisms involved in the phenotype of Down syndrome". *Mental Retardation and Developmental Disabilities Research Reviews* 13.3 (2007): 199-206.

17. Patterson D. "Molecular genetic analysis of Down syndrome". *Human Genetics* 126.1 (2009): 195-214.

18. Patterson D and Costa AC. "Down syndrome and genetics e a case of linked histories". *Nature Reviews Genetics* 6.2 (2005): 137-147.

19. Patterson PH. "Immune involvement in schizophrenia and autism: etiology, pathology and animal models". *Behavioural Brain Research* 204.2 (2009): 313-321.

Volume 8 Issue 7 July 2019