

Proteomics Congress 2018: The Era of Epigenetics: therapy influencing gene expression**Michael D Callifronas**

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Introduction:

The knowledge of epigenetical mechanisms significantly enlightens the dilemma 'nature or nurture' and constitutes a very important component for the outcome of psychiatric treatment and psychotherapeutic relationship with patients or clients who report traumatic memories and had experienced negligence or maltreatment. The story starts from the beginning in the early 19th Century, when Lamarck argued that organisms can acquire characteristics and properties through their interaction and adaptation to the environment.

Case Report

These new 'personality traits' can become lifelong stable and can be hereditated by the next generation. The term 'epigenetics' which derived from Greek, was given to this organismic property. It means "above genetics". There are two main mechanisms involved in epigenetics: DNA methylation and histone modification. A third mechanism concerning non coding RNA (ncRNA) needs to be more elucidated. DNA methylation occurs when one methylgroup (CH₃) is added on the aminoacid cytosine. This is completed through the action of a methyltransferase only when cytosine is followed by guanine, and results in long term silencing of the expression of the specific gene. It is important to note that gene methylation is a multi-step procedure, while demethylation is performed through one single step. These facts are highly important for the personality changes during psychotherapeutic interventions and psychiatry, since they show very high potential and flexibility on the multitude of lived experiences and they have a determining role in neuroplastic functions like learning, memorising and adaptive behaviour. The second mechanism concerns histone modification. Histones are proteins positively charged. Unused DNA which remains unneeded carries a negative charge and, through attraction, it is packaged around an octamer of histones. Histone molecules are subjected to methylation, acetylation or phosphorylation and can repress the genes expression by increasing the electrostatic load and tightening the coils, thus silencing DNA expression. Histone modification is transient resulting in less permanent changes than DNA methylation. The agouti mice example shows the epigenetic changes that can be observed through gene methylation without DNA modification. The mouse with a methylated gene for hair and weight has dark gray hair and is underweighted in comparison to the mouse with non-methylated gene which is yellow and normal weighted. As far as the research on Diabetes Mellitus type 2 is concerned, Dayeh et al. found about 17 genes that seem to be differentially methylated in the pancreatic islets, thus contributing to decreased insulin release after glucose stimulation.

Two years later, the same research team reduced the number of implicated genes to four. Another brilliant example of epigenetic changes is the increased methylation of the gene which controls the production of the Brain Derived Neurotrophic Factor (BDNF) in stressful environments. BDNF has a crucial role in the creation of new synapses. The reduction of BDNF production results in a decreased number of new synapses and reduced symbolisation of experiences, thus diminishing the ability to memorise and learn. In mice, stressful early life results in higher responses of corticosterone, which is the equivalent of cortisol in mice, and reduced neurogenesis in hippocampus during their adulthood. This methylation marker remains stable during life and is inherited to the next generation. So silencing of the BDNF gene, combined with the down regulation on the BDNF transcription levels are a good indicator of early life stress and abusive childhood. BDNF levels reduction in traumatic childhood may also have a teleological meaning, i.e., like a natural protection, so as to reduce accurate symbolisation of painful memories and support emotional survival. Studied the brains of suicidal children and found hypermethylation of the ribosomal RNA in the region 5' at the hippocampal area which controls the hypothalamo-pituitary-adrenal (HPA) axis. The outcome of this hypermethylation was abnormal regulation of the response to stress and suicidal tendency. In addition, Bustamante et al. found a direct relationship between the increased cytosine-phosphate-guanine DNA methylation, childhood maltreatment and Major Depressive Disorder (MDD). Oxytocin calms amygdala through reinforcement of the adducting fibers of GABA. In order to have this outcome the BDNF production needs to be increased through demethylation of the BDNF gene. Psychotherapy or relaxation or even an appropriate environment will result in this gene demethylation as will be described below.

Result

Empathic listening increases symbolization and reduces amygdala firing through activation of its middle and basolateral nucleus Uzefovsky et al. studied the neurogenetic path of empathy in participants and showed its close relationship with the oxytocin and arginin-vasopressin related genes. Schneiderman et al. found a direct relationship of oxytocin secretion with the reciprocity of the partners, their positive regard, their tender touch and their caring for the relationship. They concluded that this situation has many similarities with the mother-infant relationship and the primary attachment. Lutz et al. assert that empathy and compassion create an environment for a higher integration degree of our nervous system.

Yoga-although it is not therapy-contributes to relaxation and insight. One controlled study showed a significant increase of oxytocin in fifteen schizophrenic patients after a month of yoga exercise. It would be of interest to study the degrees of methylation of oxytocin and of BDNF gene and their relationship with empathic understanding, in order to understand the exact path to higher neurogenesis and synaptic activity. Studies examining demethylation of the oxytocin gene after couple therapy would be mostly interesting, for the neuroscience of romantic relationships. Concerning the pharmacology progress in this field, Lopez et al.

Conclusion

Cortex after an eight week therapy with citalopram. Clinical signs of depression were also improved. They proposed that the methylation demethylation procedure is a dynamic process which is included in the substrate of cognitive changes during therapy. Methyltransferase and histone deacetylase inhibitors are, at present, the main target for preparation of epigenetic drugs which will be used in mental disorders.

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