**Bringing Epigenetics into the Classroom: the Need for an Epigenetic Whiplash on Formal Education**

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**Abstract**

*We discuss the influence of epigenetic inheritance derived from school environment on the development of cognitive abilities and learning. Epigenetic mechanisms have been discovered to influence behavior and further inheritance in animals experiencing stress. Both in humans and rats evidence have shown that traumatic stress caused by an adverse environment may be inherited to the descendants. The offspring of trauma-experienced individuals expressed altered behavior and even mental disorders without the need having suffered these traumatic experiences. The cause of this heredity was not in the genome but rather in the epigenetic marks (i.e. methylations), if these marks are not deleted during the formation of gametes, permanently suppressing the anti-stress genes. Recent discoveries have demonstrated that noncoding RNAs are associated with the regulation of key neurological processes such as synaptic plasticity and the formation of the cortex of the central nervous system in children. The advent of epigenetics has revitalized neolamarkian ideas. Beside of its epistemological relevance, awareness of epigenetic marking derived from educational environment it is a must; both as a new line of research in educational academia and also in order to enrich and improve formal education. In this context, we will discuss what are the potential influences epigenetic may have in formal education and we suggest the recognition and development of Educational Epigenetics.*

Key words: Epigenetics, stress,learning, cultural inheritance, education

**Introduction**

Anyone who has watched the recent movie ‘Whiplash’ has certainly been impressed about the passion and devotion that the 19-year old Andrew puts toward excelling in drumming. However, Whiplash is much more than a movie about devotion for playing an instrument. Whiplash is indeed a movie contrasting two types of educational concepts: one that compassionate supports the individual towards learning a new skill, and that focuses on providing emotional and financial support, versus the concept of education based on selecting the ‘best of the class’ and stressfully demanding progress from she or he. What is particular about Whiplash is that Andrew is simultaneously subjected to these two types of educational models. Interestingly, in Whiplash supporters of each side could claim Andrew succeeded because of their tactics: Andrew could have exceled due to the strict education program imposed by his music teacher Terence Fletcher, or else by the love and support provided by his always present father.

Why is this discussion relevant from an epigenetic perspective?. Because strict education certainly succeeds in creating excellence, however, at a very high cost: many will drop out during the process (as it happens in the movie with even a suicide included), and the survivors that exceled will do so with a legacy or trauma in their brains, as it happens with Andrew. On the other hand, how many dropouts can be avoided by applying the paradigm of compassionate education, combined with a rich environment?. Epigenetic studies have much to say about both of these consequences, the effect of trauma and stress, and the effect of a rich environment in the long term functioning of the brain. The present paper will explore what is the role of a positive early environment on the development of cognitive abilities, and make the case that the benefit of induction and development of capabilities early in the development is far more successful and productive than applying a strong selection criteria in order to accomplish better levels of education in society.

**From Epigenesis to Epigenetics**

The term “epigenesis” is rooted on ancient Greece; with the dawn of the first ideas on organisms’ development. Aristoteles, in opposition with Hippocratic School’s preformist ideas, postulated that embryo organs were originated during development (Muller & Olsson, 2003). During XVII, William Harvey in his pioneering book “Exercitationes de generatione animalium” used the term epigenesis in order to explain organisms’ development from unstructured germinal matter. Later, Waddington (1942), using his metaphor “Adaptive Landscape” to refer to epigenesis as a concept to explain causal interactions between genes and its products, generating phenotypes through cell differentiation mediated by genetic regulation (Slack, 2002). This conceptual achievement gave rise to Epigenetics (Waddington, 1942; Van Speybroeck, 2002). These revolutionary ideas did not flourished in the following years, mostly because most researchers were focused on Mendelian inheritance, only finding its rebirth with recent advances in molecular biology (Jamniczky et al., 2010). The technological advances gave strength and further empirical support to Waddington ideas and the relevance of epigenetics have reached out the academic discussion and it is becoming a relevant factor to discuss issues of public concern from human health and welfare to globalization and global warming crisis (Portela & Esteller, 2010; Baylin & Jones, 2011; Guerrero-Bosagna & Jensen, 2015). The goal of the present work is to provide a historic revision on the link between epigenesis, epigenetics and neuroscience exploring the implications of epigenetic dynamics on formal education, and opening the discussion on the space concerning the epigenetics of education.

**Foundations on Behavioral Epigenesis**

North American psychologist James M. Baldwin was one of the first in to discuss behavioral epigenetics when we proposed the term “organic inheritance” (Baldwin, 1896, 1897). Baldwin was interested on the hereditary bases from the development of some intellectual skills in children such as memory, reasoning and language; As well as how these may relate with social development and its potential consequences on behavior evolution (Bloom, 1986; Broughton, 1981). Baldwin attempted a reconciliation between Darwinism and Lamarckian ideas. He argued that individuals’ habit to learn may guide evolutionary processes. Cultural inheritance from a learnt behavior during several generations may become a genetically based behavior. In other words, epigenetic condition of an individual may arise by means of natural selection. Skills initially requiring a learning process to develop would be replaced trough the evolution of a genetically determined system with no need of further learning (Baldwin, 1896, 1897; Loredo, 2004; Lorendo & Sánchez, 2004).

Baldwin ideas were opposed to Weismann’s whom postulated a drastic differentiation between germinal cells and somatic cells, proposing the existence of an unbreakable barrier between these two kinds (“Weismann barrier”, reviewed by Winther 2001). On his perspective, biological inheritance was located only in germinal cells and any kind of chance suffered by somatic cells will not be transferred to the following generation. However, now it is recognized that there exist mechanism allowing stress and other environmental pressures experienced through ontogeny to affect inheritance, revisiting Baldwin idea.

Despite its contribution, epigenesis of behavior and learning is more often associated with the works of Piaget than with Baldwin’s. This is due to the big steps advanced by constructivism. Piaget used Waddington epigenesis concept to explain some aspects of human behavior and its core relevance on animal behavioral evolution (Genovese, 2003; Piaget, 1970). An environmental factor is assimilated by genotype in a way that it became independent from its environmental inductor, this process was previously considered by Waddington whom coined it as “genetic assimilation” (Waddington, 1953). Piaget extrapolated this concept for the psychological level labeling it as “cognitive assimilation”, meaning that no knowledge is a copy of real world because it always involve a process of assimilation of previous structures (Piaget, 1969). Assimilation, as described above, plays a key role in any knowledge acquisition process. When a child perceived an object, identified it as belonging to certain conceptual categories previously defined by its perception (Piaget, 1969). Piaget also took the idea of epigenetic landscape or “creodas” de Waddington to its cognitive discussion. This idea, as mentioned before, proposes that during development exist differentiated routes linked to the development of different organs. For Waddington, all embriogenic process depends on a network of genetic interactions and not to the action of particular genes; he states as unacceptable the idea of genetic determinism. Piaget welcomed such approach and postulated that adaptive landscape for cognitive functions suppose a tight collaboration between environmental factors and genome. Therefore, for Piaget, genetic epistemology consisted in to explain the construction of knowledge, of psychological functions and “intelligence” during development through interrelated mechanisms where cognitive assimilation, epigenetic landscape and adaptation of species to its environment play a preponderant role (Piajet, 1969, 1970).

This channeled construction of knowledge is what makes the individual more capable to seek for solutions to problems faced by his environment. Extrapolating some of these concepts to the classroom, in it each student structures his knowledge of the world based on a common unique pattern presented by the teacher. They connect every single fact, experience or understanding of information in a new structure that grows in a subjective manner, leading the student to establish significant relationship with the world (Abbot & Ryan, 1999; Eshach, 2007).

Recent thinkers on the construction of cognition remark the dynamic characteristic of these behavioral processes (Oyama, 2003). As Waddington and Piaget she also refused the distinction between nature-nurture and the prevalence of a genetic preponderance for explaining human psychology. Instead Oyama defines cognitive processes as developmental systems and stress out the existence of dynamic emergent controls that help to understand acquired phenotypic modifications through both evolutionary and ecological contexts. These controls emerge during the interaction of organic organization, through the hierarchical levels of behavior and cognition in time. To our approach learning and formal education fits to Oyama’s notion of developmental systems and are subject to the dialectical flux between levels explaining its phenotype and hereditary consequences for our species, where in addition to evolution and ecology socioeconomic factors must be considered on behavioral development and learning (Hackman et al 2010).

**Modern Epigenetics, Mechanisms and Inheritance**

Initial propositions addressing the link between genotype and phenotype hypothesized a more or less linear functional connection among them, where the phenotype was the result of the interaction of genes with the environment. This constituted the classical proposition of Mendelian genetics. In this framework, phenotype is the result of a “genetic program” located in a coded area of genome. Based on this proposal, “norm of reaction” and “phenotypic plasticity” will never be a part of organisms inheritance system. However, recently a mayor scientific achievement changed this previous paradigm; the demonstration of the existence of small ribonucleic acid molecules not bearing any proteosyntetic function, called non-coding RNAs (ncRNAs). (Ghildiyal & Zamore, 2009; Guil & Esteller, 2012; Jacquier, 2009; Pauli, et al. , 2011).

These ncRNAs derived from messenger RNAs (mRNAs) (introns) and they were considered to be part of the so-called “genetic junk” (Muotri et al., 2007). Later, considerable amounts of ncRNAs were also discovered in retroviruses, retrotramposons and non-coding sectors of DNA. Most striking of all was the discovery that, these ncRNAs were able to regulate gene expression similarly to proteins (Wang et al., 2008), and their altered function gives rise to diverse hereditary maladies, such as neurological disorders (Vučićević, et al 2014). In multicellular organisms, cell types differentiate during development in order to form organs associated with specific capabilities. In each cell type originated during development specific ncRNAs are transcribed and epigenetic patterns are established. In these cell type-specific epigenetic patterns are composed of epigenetic marks such as histone modifications or DNA methylation (Keller & Bühler, 2013), which are able to “switch off” genes that are not in use in a given tissue (Cabianca et al., 2012), while “switching on” genes involved in specific functions in these derived cells (Fatica & Bozzoni, 2014; Guttman et al., 2011).

The identification of crucial developmental periods of major epigenetic reprograming in laboratory rodents was a fundamental step in epigenetic research (Hackett & Surani 2013a). Two developmental periods exist in which major epigenetic changes occur in the genome of mammals (Hackett & Surani 2013a, d). One of these periods is after fertilization, where a reduction in methylation occurs followed by re-establishment of methylation patterns by the time of blastocyst implantation (Hackett & Surani 2013d). This epigenetic reprogramming is crucial for the differentiation of somatic cells lines.

Another period of epigenetic reprogramming, which is of high relevance for the germ line, occurs during the migration of primordial germ cells (PGCs) towards their final establishment in the gonads (Allegrucci et al. 2005, Lees-Murdock & Walsh 2008). During this migration a major demethylation of the genome also occurs followed by re-methylation (Hackett & Surani 2013a, Lees-Murdock & Walsh 2008). Periods of resetting of DNA methylation patterns, either in early embryos or PGCs, are windows of sensitivity to environmental exposures (Feil & Fraga 2011, Jirtle & Skinner 2007). Interfering with the resetting period of PGCs, however, has different implications than interfering with the resetting period of pre-implantation embryos. Because the germ line has the ability of transmitting epigenetic marks to next generations, altered DNA methylation patterns produced in the germ line after interferences with this epigenetic reprograming can be transgenerationally perpetuated (Skinner et al. 2010). This is described as the phenomena of transgenerational epigenetic inheritance (Daxinger & Whitelaw 2012, Grossniklaus et al. 2013).

Recent investigations show that several diseases of common occurrence in human populations are not inherited in a Mendelian fashion, but through transgenerational epigenetic inheritance (Guerrero-Bosagna & Jensen 2015). These environmentally-induced diseases, which are transgenerationally transmitted, include obesity, polycystic-ovary syndrome or male fertility impairments (Anway et al. 2005, Guerrero-Bosagna & Skinner 2014, Guerrero-Bosagna et al. 2012, Nilsson et al. 2012, Skinner et al. 2013).

Recent reports have also shown that not only developmental exposures but juvenile or adult exposures could also produce alterations in the germ line with consequences in future generations. Examples of this phenomena include: exposure of juvenile male mice to low protein diets, which produces alterations in the liver transcriptome of the offspring (Carone et al. 2010); fear conditioning of adult male mice with an odorant, which has consequences in the neural anatomy in the next two generations (Dias & Ressler 2014); and paternal stress in male mice, which affects the hypothalamic–pituitary–adrenal (HPA) axis and micro RNA expression in the offspring (Rodgers et al. 2013). In all these cases the transgenerational transmission of the effects is mediated by epigenetic alterations in the paternal germ line.

**Epigenome and Epimutations affecting Behavior**

The relevance of epigenetic processes in synaptic plasticity, learning, and memory has recently been demonstrated, in different model organism (Mundinger, 1995; Kramer et al., 2011). It has recently been shown that memory stabilization in postmitotic neurons is linked to epigenetic mechanisms in cell differentiation and development (Day & Sweatt, 2011a) with memory formation and maintenance being related to changes in DNA methylation patterns (Day & Sweatt, 2011b). For instance, early life stress has been demonstrated to persist due to these processes been capable of affecting learning and memory capabilities (McClelland et al., 2011).

Epigenetics not only explain the emergence of phenotypic plasticity, but also the inheritance of these environmentally induced characters. Phenotypes correspond then to genotype dialectic with epigenotype with the contribution of environmental factors (Frías-Lasserre, 2012). Modern epigenetics consider the molecular changes influencing genetic expression without modifying the DNA sequence; These changes include DNA methylation and chromatin’s histone modification (acetylation), RNA silencing mediated by ncRNAs, RNA editing, epi and paramutations (Morgan et al., 2005; Probst et al., 2009; Gonzáles et al., 2011). Many of these changes are sensitive to environmental cues (Li et al., 1993; Reik & Walter, 2001; Salmon et al., 2008; Jablonka & Raz, 2009; Johannes et al., 2009; Koerner et al., 2009; Verhoeven et al., 2010; Daxinger & Whitelaw, 2012; MacDonald, 2012; Frésard et al., 2013).

Recently, Isabele Manzur and collaborators from Zurich University have demonstrated that traumatic stress can be inherited in rats. In this experiment (2014), newborn pups were separated from their mothers during two weeks. During that time they reacted in a very dramatic way to their mother’s separation developing depression symptoms and antisocial behaviors when reaching adulthood, been incapable of facing adverse or novel circumstances. Such traumatized rats preserved their altered behavior during all this life and transmitted them to their offspring, demonstrating that these aberrant behaviors were kept for the next three generations (Gapp et al., 2014). Also in our own species it is been demonstrated that infancy´s posttraumatic stress, beside of modifying subject’s behavior and generating psychological disorders, may also became inheritable to offspring (Taha et al., 2014).

Behavioral changes are also shown to be related to disruption of genomic imprinting, which correspond to epigenetic marks that are differentially established in each parental allele, inducing parental-specific expression in diploid cells (Reik & Walter, 2001). Due to imprinting, the expression of some genes is restricted one of the alleles. Alteration of imprinting in these genes may contribute to the development of neurobiological disorders such as psychosis and autism (Isles et al., 2006; Úbeda & Gardner, 2010, 2011, 2012). Studies in rodents have described genomic imprinting related with parental care (Wilkins & Haig, 2003; Wolf & Hager, 2006). Regarding epigenetic trauma affecting behavioral epigenesis, it has been demonstrated that early-life adversity remains as a perdurable epigenetic marks at the brain-derived neurotrophic factor gene in the central nervous system (Roth, et al. 2009).

In another work, unpredictable maternal separation induces depressive-like behaviors and altered behavioral response to aversive environments in isolated adult animals due to DNA methylation alterations. Moreover, these behavioral alterations were further found in the offspring of males affected by maternal separation. With disregard that that these males were reared normally, DNA methylation pattern linked to altered gene expression were also present in these generation(Franklin et al., 2010). These researches demonstrate the relevance of epigenetic molecular mechanism leaving lifelong and possible transgenerational perpetuation of changes in gene expression and behavior epigenesis incited by early trauma and stress

In 2014’s Gapp and collaborators studied the number and kind of a specific ncRNA (microRNAs) expressed in adult rat cells exposed to traumatic conditions during early life and compare them with non-traumatized rodents. They discovered that traumatic stress was capable of altering the amounts of microRNAs in blood, brain and spermatozoids. Some of these were produced in excess while others were underrepresented in comparison with control animals. These changes were result of a deficient regulation of cell processes controlled by these microRNAs. As explained before, following traumatic experiences during infancy, adult rodents behaved quite different from control showing depressive behaviors. These behavioral symptoms also occurred in their offspring’s, despite these pups were never exposed to stress in their ontogeny, suggesting that these traumatized pattern was inherited trough the epigenetic marking on parental’s spermatozoids.

Together with spermatozoid`s microRNAs imbalance a key factor in trauma transmission was discovered, however, some questions are still open. For example, how does short RNA deregulation occur? Most likely is that this is a part of a chain of events beginning with the production of excesses of stress hormones (Gapp et al 2014). In these experiments, decedent’s metabolism from stressed rats also was affected: insulin levels and blood ‘s sugar were lower than controls. With these evidences it was first demonstrated that stress-affecting metabolisms may also be trangenerationally transferred through epigenetic inheritance, even to the third generation. It is important to highlight that acquired traits, different from the ones incorporated through stress, may also be inherited by similar mechanisms as the one studied by Gapp and collaborators. Surrounding environment leave footprints in human brains, organs and also gametes. Through these effects, these marks may even pass to the next generation (Gapp et al. 2014).

These mechanisms and examples of transgenerational epigenetic inheritance on behavior and cognition remark the relevance of incorporating these knowledge not only as additional chapters in school teaching but in the development of educational policy, considering how environmental pressures may affect students and its parents as active parts of the success of formal education. The following section focus on our ideas related to this topic.

**Relevance of Neurobiological Epigenetics in Education**

Neuroscience and its application to education is an emerging interdisciplinary field that integrates brain functioning, pedagogy and education (Sigman,et al 2014). This assembly has triggered a true revolution in educational research and practicing (Goswami, 2006), however, there still a need to fill the gap between science and school life in order to incorporate the latest discoveries on behavioral and psychological epigenetics to improve and effectively impact formal education (Howard-Jones, 2014). Genes are involved with epigenetic mechanisms during brain development and its functional configuration (Singer, 2008; Fagiolini et al., 2009). Therefore, the epigenetic component of brain dynamic during learning and memory formation must be considered by educational neuroscience research and application (Gräff & Mansuy, 2008)(Levenson & Sweatt, 2005, Day & Sweatt, 2011a). On top of this ontogenetic developmental process are the potential epigenetic transgenerational effects earlier discussed, thus epigenetic influences may be pervasive.

Paraphrasing Susan Oyama, the configuration of the educational process it is a developmental system itself where students and its surrounding environment constitute a unit of dynamic development (Oyama, 2000). This is why defining what it is the objectives of formal education are basic in order to design appropriate programs considering neurobiology and epigenetic effects on students and its family.

As mentioned above, many studies show the inheritance of environmentally-induced nervous system pathologies. However, Mendelian genetic has been unsuccessful in providing an adequate explanation to the inheritance mechanisms related to the etiology of these diseases, as most of them are they were not shown to be determined inherited in a Mendelian fashion. Additionally, it is known traumatic experiences may induce behavioral disorders capable to be transferred to the offspring, as discovered by Gapp et al (2014).

 Nonetheless, its mechanism of transmission was not clear neither it was possible to associate specific genes to these phenotypes. Only after the advent of molecular genetics is when the mystery of altered behavior’s heredity is been disentangled. Now we are aware that epigenetic mechanisms play a preponderant role. This, because different types of these molecules are transcribed to some tissues and there they play a particular role; and when this role is altered they cause diseases (Niland et al., 2012; Fenoglio et al., 2013)

In the last years it has been described that mRNAs and micro RNAs play a major role in neural and synaptic plasticity in mammals(Burke & Barnes, 2006; Vo, Cambronne, & Goodman, 2010). This is explained by the regulatory effect of micro RNAs over dendrite morphogenesis during early development (Kosik, 2006; Smalheiser & Lugli, 2009; Bredy et al., 2011; Fenoglio et al., 2013). Some RNAs (si RNAs) show a drastic augmentation during learning early stages, these have been suggested as relevant on the expression of neuropsiquiatric diseases (Smalheiser & Lugli, 2009; Spadaro & Bredy, 2012, Roth, et al 2009). All this evidence demonstrates the relevance of developmental environment and transgenerational epigenesis and epigenetics for an adequate achievement of cognitive goals such as formal education and learning (Galván, 2010), remarking the adequacy of considers the educational process as a developmental system (sensu Oyama) where parental health is part of the fundamental inheritance where the bricks of further experience acquisition will be cemented. In addition, this developmental system must consider learning and its cognitive process in its epigenetic dimensions allowing students to achieve these goals and construct their significant meanings on their brains in a suitable environment for brain development, especially in their early stages of structural organization.

Because all these epigenetic-related advances are changing the foundations of behavioral sciences and neurobiology, it is paramount that these novel concepts that emerge are incorporated into the teaching philosophy at the levels of basic and high schools.

**Discussion and Future Developments**

Epigenetics is a new discipline derived from genetics that include the environmental context as relevant part of heredity. This science branch is shaking the foundations of Medicine, Psychiatry and Psychology and without doubt will have an impact on Educational Sciences through Neurosciences. In order to understand and ponder the relevance and transforming power of these epigenetic processes it is necessary to incorporate the epigenetic component in to the regulatory processes occurring in our central nervous system (Day & Sweatt, 2011b). When education researchers will achieve this, its transposition to policy makers cannot wait.

It is necessary to extrapolate these brain-developing factors both in the concepts to be teaching in school education and Universities. Actions must be considered in order to ensure fair conditions for memory and learning development from early children to adulthood. It will be a must to regulate and norm that educational institutions have the adequate environmental conditions for an enriching and healthy educational process. In this way all actors involved in the educational system will contribute in to education goals and in to the prevention of cognitive and psychiatric disorder in students with potential hereditary consequences, as explained above.

Statements such as “La letra con sangre entra”, sort of like “Characters (letters) are learnt with blood” classically repeated by Sarmiento’s school for education in South America (reviewed by Carli 2014) and kept nowadays changing instead of “blood” its legal synonym “rigor and stress” for students as a positive factor contributing to their significant learning must be erased from the formation of future teachers and school educators. This, in consideration to the effect of traumatic experiences both in the cognitive processes and students’ future mental health (Prinzie et al., 2004) and its hereditary consequences suggested by last findings in rodents.

Therefore, serious efforts must be emprise in order to gain awareness of the different controls and influences shaping the outcomes of school teaching and, furthermore, the potential influences of these experiences on the future cognitive development and heredity kept by the subjects of such educational processes. Epigenetic of education is going on, and we have to consider it as part of the equation on formal education.

Inadequate learning environments may affect the pathways on the underlying developmental process. As explained with nowadays evidence from epigenetic studies, these stress factors and unhealthy environments may alter the formation of neural circuits, affecting the acquisition of abilities linked to learning and generate epigenetic marks on students gametes with potential disastrous consequences for the mental heath of their sons and daughters. Epigenetic processes are a scientific fact and must be incorporated to our educational reality in order to be able to consider their potential values and use it in favor of a better educational system. Current progress have to be acknowledged, such as The Moore Institute School of Medicine with its “Lets get Healthy” initiative (www.letsgethealthy.org), which incorporate epigenetic dimension on Middle school program, as a way to considerate these field in to educational backgrounds.

We propose efforts must be concentrated in to develop multidisciplinary research and dialogue between educators and scientist in order to construct an applied field focused on education: Educational Epigenetics.

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