Proactive epigenesis and ethical innovation: A neuronal hypothesis for the genesis of ethical rules.

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Proactive epigenesis and ethical innovation

A neuronal hypothesis for the genesis of ethical rules

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During the long period of postnatal development in humans, the cerebral cortex undergoes intense synaptogenesis, which persists into adulthood. The steady interaction with the physical, social, and cultural environment drives an epigenetic selection of neuronal networks to internalize, in particular, the common cultural and ethical rules of the society to which the child and her/his family belong. Based on this knowledge, we propose the idea of proactive epigenesis to develop new ethical rules and educational approaches to influence, and constructively interact with the developing neuronal architecture of the human brain.

Synaptic epigenesis

Conrad Waddington used the word epigenesis to describe how genes interact with their environment to produce a phenotype; in other words, how the inherited potential of the genome develops into an adult organism [1]. This definition was applied by Changeux *et al* to the developing brain, assuming that, throughout a sequence of nested developmental stages, the environment leaves characteristic "prints" in the connective organization of the child's brain [2]. At each of these elementary steps, the synaptic network in the brain first becomes transiently larger and less specified than in the adult; the activity of the network—spontaneous or evoked by the outside world—then regulates the stabilization and degeneration (pruning) of labile synapses.

This theory was an attempt to explain the paradox of nonlinear evolution of brain-vs.-genome complexity. From the mouse (75 million neurons, with about 100 billion synapses) to the human brain (85 billion neurons, with a million billion synapses), the complexity and organization of the brain have dramatically increased, whereas the number of coding genes in the genome has remained almost constant at 20,000–25,000 structural genes in mouse, monkey, and human and the sequence differences in these genes are rather small. Moreover, the postnatal period of brain maturation is much longer in humans than in any other species and can last from 15 to 20 years. During this extended period, critical and reciprocal interactions take place between the developing brain and its physical, social, and cultural environment. The brain progressively builds its adult connectivity through a constant dialogue between the genetic endowment of the child and her/his experience of the external world. The postnatal period thus involves a trans-generational transfer of information from adult to child through the internalization of the social and cultural environment in the child's brain.

> *"The brain progressively builds its adult connectivity through a constant dialogue between the genetic endowment of the child and her/his experience of the external world"*

This definition of *synaptic epigenesis* differs from genomic epigenesis: the status of DNA methylation and histone modification of particular regions of the genome that is associated with interactions with the outside world. The main difference is that the latter takes place at the level of chromatin, while the former deals with a much higher level of organization, namely between nerve cells, and involves an average of 10,000 synaptic contacts or more per neuron. One does not expect genomic epigenesis to account for language acquisition or cultural diversity.

The mathematical formulation of the theory of synaptic epigenesis establishes an important theorem of variability and states that "different learning inputs may produce different connective organizations and neuronal functioning abilities, but the same behavioral ability" [2]. In other words: The neuronal connectivity exhibits degeneracy in the sense that several *code* words or patterns of connections have the same meaning (function). The theorem thus predicts that the synaptic connectivity between genetically identical individuals, such as monozygotic twins, would be different, which was demonstrated using serial EM microscopy in the 1970s. Another piece of experimental evidence is that both the evoked and spontaneous activities of a developing neuronal network increases the elimination of connections, whereas blocking the network has the opposite effect, as shown, for instance, with the neuromuscular junction by Changeux and colleagues, or on the visual system by Shatz and colleagues. Lastly, as illustrated by the early work of Wiesel and Hubel, interactions between the developing brain and its environment leave traces, which last almost irreversibly until the adult stage. Another, well-documented example is amblyopia, which when left

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untreated, results in decreased vision in one eye at the level of the cerebral cortex caused by abnormal vision during childhood.

The genesis of epigenetic rules

From a neuroscientific perspective, ethical and social norms may therefore be conceived as spatiotemporal patterns of neuronal activity that can be mobilized within the conscious neuronal workspace and stored as long-term traces in brain memory. The brain networks involved in the selection of these epigenetic patterns are being identified by studies of neurological deficits, which point to the lateral prefrontal cortex. In more general terms, the prefrontal region of the cerebral cortex acts as a "temporal buffer" between past events and future actions and contributes to decision-making within the context of the individual's history. In such a neuronal workspace, "neurally encoded rules" associate a context with a specific behavioral response in a top-down manner [3]. This is referred to as cognitive control and coordinates thoughts or actions in relation to internal goals. Brain imaging fMRI revealed a hierarchical cascade of executive processes, which are implemented in distinct regions, from posterior premotor to rostral lateral prefrontal cortex, typically Brodman's area 46 [4]. Behavioral rules are sorted at these nested levels of information processing, the highest-level ones controlling the underlying ones closer to the senses. Although Koechlin and colleagues did not explicitly mention social interactions in their original papers, we may extend their model by assuming that ethical or social norms control rules and part of the "concurrent behavioral strategies" in decision-making [4].

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From birth on, and possibly even prenatally, the baby is exposed to a social and cultural environment. During its development, an epigenetic selection of neuronal networks accompanies the acquisition of the ethical rules of the social community to which the child and her/his family belong. These ethical rules are often linked with symbolic representations of the cultural community, and the acquisition of such ethical rules and symbolic systems has been compared to language acquisition. Against this background, we propose the possibility of *epigenetic proaction* and developing new ethical rules to influence and constructively interact with the developing neuronal architecture of children's brains.

The meaning of epigenetic proaction

The human brain develops within a species-specific "genetic envelope", with important neural plasticity available to respond to environmental influences and self-experience. Yet, our brain architecture possesses innate evaluative predispositions, such as self-interest, control orientation, dissociation, antipathy/sympathy, and empathy [3,5], which show some universality across the human species in spite of a vast phenotypic variance at both individual and cultural levels. Epigenetic development would further develop these innate dispositions in one direction or another, depending on the context. "Favouring a model that lays emphasis upon the spontaneous activation of the violence inhibitor and of the moral emotions of empathy and sympathy in the course of development [...] lends support to the thesis that these dispositions are intrinsic and innate properties of the human brain- in other words [...] properties of 'being born human'" [3].

There are two messages here. First, we are neurobiologically predisposed toward specific values, such as self-interest, empathy, sociality, and so on, and our brain structures develop in response to ethical and social norms in our cultural and social context. Second, given neuronal plasticity and the underlying epigenetic mechanisms, we may influence, both biologically and culturally, how the brain responds to and constructs ethical and social norms. The fundamental idea of epigenetic proaction is therefore trying to understand and influence the genesis of new ethical and social norms in light of what we know about the brain. Being epigenetically proactive also means adapting and creating social structures, and even institutions, to constructively interact with the developing neuronal architecture of our brains. This can be described as an educated form of *ethical innovation*. The scientific challenges involved are accompanied by important social and ethical responsibilities [5,6].

Neuralization of social norms

The human species spends a considerable part of its lifespan developing its brain by experiencing and appropriating its physical, social, and cultural environment. In fact, environmental influence on the brain's functional architecture yields an evolutionary strength to *Homo sapiens*, compared with other animals whose brain developmental period is comparatively much shorter, and less determined by environmental factors. Moreover, trans-generational transfer of information takes place through the incorporation of the social and cultural environment in the developing infant brain. Accordingly, culture evolves along with us and it can help us in the construction of our brain. Conversely, through creative and rational thinking, our brains may lead to the production of novel social structures that persist across generations, and which might be stored in extracerebral memories as inscriptions, codes, or laws.

> *"Our cultural and social structures [...] are important products of the neuronal structures of our brains, but these neuronal structures are also important products of our cultures and societies ..."*

In view of this neurobiological–cultural symbiosis, we can describe this process both as a "neuralization" of the normative process itself, and as a "culturalization" of the brain through the selective stabilization of neuronal circuits. Our cultural and social structures—including our normative reasoning—are important products of the neuronal structures of our brains, but these neuronal structures are also important products of our cultures and societies, and their history. Hence, the possibility to influence our brains with the use of culture, and be epigenetically proactive, in other words: to invent, learn, and transmit new ethical norms, forming some kind of new ethical languages. An important challenge for a

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joint approach of both natural and social sciences, and humanities, is to decipher the network of causal relations between these perspectives. Notably, to determine what factors influence the developing child, how they influence him/her, and what types of influence may become irreversible.

Ethical innovation

Human diversity poses challenges to the implementation of epigenetic proaction. Diverse systems of rules and norms have developed in distinct societies and historical eras often in strikingly different cultures. No doubt, epigenetic proaction, if applied, might emphasize diverging values in distinct cultures. Yet, it is conceivable that some common core could be found or created.

> *"If new cultural circuits, such as a better ability to control violence, become epigenetically stored in our brains, more peaceful societies might hopefully develop"*

Whether or not it may be possible to develop universal ethics, or whether this is even a desirable goal, a modest quest for universally shared values could be defended, for example, in terms of the survival of humans as a species, of other species, of the planet, but also in terms of "the good life" [3]. The theory of epigenetic proaction suggests that we may be able to facilitate evolution in the desired direction, implementing selected values that are adequate to the future of the human species on a universal scale. One area of particular importance deals with the persisting economic contrast between countries from the North and from the South, and the scientific study on how poverty and illiteracy influence the development of a child's brain [7].

In addition to challenges with cultural and social diversity, time also presents a challenge. If new cultural circuits, such as a better ability to control violence, become epigenetically stored in our brains, more peaceful societies might hopefully develop. But here we face a problem of circularity: In order to maintain social nonviolence, we already need to be nonviolent. It is unlikely that a society that embraces violence could stabilize nonviolent cerebral features. The question arises: How long does it take for a cultural characteristic to spread in a society and leave a stable cerebral imprint? Some enduring cultural structures are needed in order to cause broadscale neurobiological changes and store cultural imprints in the brain, but the chances of maintaining societies that conflict with the present nature of its inhabitants are arguably slim [5,6].

At this point, we may consider: Is ordinary education enough? Do we need to know and possibly modulate our biology in order to achieve a "better", or a "good" life? Our short answer is that education is precisely what epigenetic proaction is about: It is an educational program and, as with all educational programs no matter how we choose to label them, it influences the brain. What distinguishes the epigenetic educational program is mainly that it is explicitly aimed at favouring individuals as well as cross-generational transmission of ethical/social norms on the basis of our knowledge of the brain.

> *"... epigenetic proaction would focus on novel educational/management programs with long-term influences across generations..."*

This impacts how society structures education from kindergarten, through primary school, to high school, and so on. For example, the timing of teaching particular subjects in school can be adapted to the level of wakefulness a child normally experiences at different times of the day. For instance, children are typically less alert in the morning, so teaching mathematics should ideally take place later in the day. Another question is whether or not it is appropriate to teach several languages simultaneously or sequentially during early development. Learning written language is a difficult "un-natural" task for a five-year old, and using experimentally tested neurally based strategies may improve the acquisition of reading and writing skills. In moral education, inspiring models and gentle encouragement may have stronger positive effects than previously imagined, whereas violence, for example, corporeal punishment, may have detrimental effects that could irreversibly damage the child. Another issue is the cultural differences between individual children. Using open critical debate, educators could teach that these differences are circumstantial brain traces and secondary in importance to belonging to the human species. Epigenetic proaction is not normative in itself, but suggests that cultural norms and early childhood experience can have a far deeper biological impact than traditionally assumed. Like all knowledge, epigenetic proaction can be misused, and several ethical issues need to be addressed in this context.

Ethical issues

Human society has developed considerably since ancient times: Social rights, gender equality, environmental conscience, and poverty alleviation have improved the human condition. Unlike previous generations, we have the knowledge and the practical means to abolish famine, establish global health care and education, and remedy environmental degradation—but we also have a unique capacity to build weapons of mass destruction and eliminate populations, societies, and even the planet and life upon it. We need to recognize—we even have the responsibility to recognize—not only the advances we have made, but also the risks we face that have increased with our development. One of the motivating forces behind our suggestion for epigenetic proaction is a concern about the present state of the world, and the difficulties in dealing with the situation adequately.

> *"The notion of "improving" the human condition must be evaluated with great caution, since it has some very sordid versions."*

A similar concern arises in the current debates on "moral enhancement". It is often argued that human nature is not able to deal with the problems that human kind presently faces in part as a result of our own actions—environmental destruction, poverty, and so on—and that moral education has not been able to forestall the

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present global situation. Another similarity between these two discourses lies in the belief that human nature could be "improved", much to the benefit of our societies. The main differences between these approaches are the suggested solutions, and the methods used to achieve them.

In the "moral enhancement" debate, the focus is largely on the individual, and the methods suggested are often a "quick-fix" of the brain, such as drugs, gene/cell implants, or brain stimulation, ignoring the potentially dangerous short- and long-term consequences on human brain function. In contrast, epigenetic proaction would focus on novel educational/management programs with long-term influences across generations and make no reference to the direct and blind "artificial" interventions on the brain. Epigenetic proaction can have important effects on the individual person, and on the individual generation, but it is not conceived as an individual shortcut in the same way that moral education is.

Since epigenetic proaction is a process on the societal level, it is not an individual opt-in/opt-out matter. When educational structures are being adopted in a democratic society, or when laws are being passed, people are invited to express their views through political elections, public debates, consensus conferences, and so on, but they are not invited to opt in or out; we do not ask each citizen for informed consent. The implementation of epigenetic proaction in a specific society would likewise be a matter for public debates and political decisions, not for individual decision-making.

Social engineering?

Would epigenetic proaction be a "social engineering" project, since it recommends the use of scientific methods to analyze, understand, and influence social systems? That term has negative connotations: Social engineering has often been attempted in dictatorships to create a society dominated by "good citizens", or racially or ethnically "pure" people. The notion of "improving" the human condition must be evaluated with great caution, since it has some very sordid versions. Historic awareness is essential to preventing scientific ideas from being hijacked by nefarious ideologies and abused for unscientific purposes. Even the most objective science can be misinterpreted to suit diverse ideological and political agendas, and a socioscientific program of epigenetic proaction would likewise have to take this risk into account.

Here, we would like to make a plea for introducing secularity or "laïcité" in educational systems throughout the world, wherever possible. The absence of religious involvement in education, especially the abandonment of religious influence in the determination of educational policies, is not an anti-religious norm, but refers religious creed to the private realm, where it should be respected. Dogmas—especially but not exclusively religious ones—may contribute to societal conflicts and wars: If children are exposed early in life to secularism and normative diversity, communitarian fanaticism and extremism may become less prone to develop. They may still arise because many different factors determine this, but one important factor, namely early childhood indoctrination, has at least been reduced.

Trying to understand and build up human norms in light of what we know about the brain and its development is a great scientific challenge accompanied by important social and ethical factors. Research collaborations between neuroscience, genetics, and social science provide rich and multifaceted knowledge about the human condition and an increasingly integrated view of us as biological organisms interacting in complex natural and cultural environments in constant evolution.

The human brain is slowly beginning to understand itself. That is historically unique, and we are still at the beginning of this process. How we shall react to and use it is a matter of more or less informed conjecture and choice. In the dawn of this new enlightenment, vigilance is needed yet need not quench optimism. We may choose to use our power well and develop, biologically, as well as culturally, into whatever we regard as "better educated" creatures constructing more advanced societies. The values we select and the methods we choose to obtain them will determine how and whether neuroscientific and philosophical enlightenment in the form of epigenetic proaction shall improve or aggravate the human predicament.

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Conflict of interest
The authors declare that they have no conflict of interest.

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