

Role of Hippocampal Prenatal Imprinting and Social Outcome in the Pathogenesis of Depression

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Abstract

Diverse knowledge have been learned from eusocial insects like the ants. The division of labor, characteristic of eusocial species, is a consequence of the social needs of these insects, and is determined by pheromones influences. Now we may consider that the human species is eusocial. Changes of the individual as consequence of social needs, may be determined by maternal prenatal imprinting. Fetal hippocampus may show modification in the hormonal and neurotransmitter receptors as consequence of the influx of maternal stimulus. Thus, human individuals may have a form of social programming. If the society is modified after birth, the organic brain substrate enters in a situation of discordance. This discordance, according to this hypothesis, may trigger changes in the mental sphere including a form of chronic organic depression.

Keywords: Prenatal imprinting; Depression; Eusocial species

Introduction

Etiology of depressive disorders is still unknown [1]. Several factors are involved in the pathophysiology of depression such as genetic changes, neurotransmitters and neuroendocrine alterations, life events and social difficulties. The role of maternal imprinting in the cerebral development of the fetus as response to diverse forms of social stress, should be considered in this pathophysiology. *Homo sapiens* may be a eusocial species [2], which is a form of social evolution when the work is divided between individuals. The individuals differ and are distributed in the population as consequence of a social response. The works of Edward O. Wilson in ants show the base of this theory. We postulate that individuals are imprinted from the prenatal stage to meet social needs. Environmental and social postnatal changes, may determine serious discrepancies between the cerebral imprinting determined by the mother, and the real function which is faced by the individual in society. This discrepancy can generate a form of individual organic depression.

Role of Evolution in the Social Behavior

Brain development and what we call intelligence is part of an evolutionary feature of the human species. Diverse social aspects are due to evolutionary changes at brain function. These approaches have led to the study of changes in many genes. Per example, genes associated with language and speech (forkhead box P2 (FOXP2), protocadherin 11 X-linked (PCDH11X) and PCDH11Y), genes associated with brain size (microcephalin 1 (MCPH1), asp homologue, microcephaly associated (*Drosophila*) (ASPM), CDK5 regulatory subunit associated protein 2 (CDK5RAP2), solute carrier family 2 (facilitated glucose transporter), member 1 (SLC2A1), SLC2A4, neuroblastoma breakpoint family (NBPF) genes, growth arrest and DNA-damage-inducible gamma (GADD45G), ret finger protein-like 1 (RFPL1, RFPL2 and RFPL3) and genes associated with neuronal functionality (dopamine receptor D5 (DRD5), glutamate receptor, ionotropic, NMDA 3A (GRIN3A), GRIN3B and SLIT-ROBO Rho GTPase activating protein 2 (SRGAP2) [3]. A correlation with human technology and culture develop has been linked. Thus, aspect as first stone tools, expansion to Eurasia, control of fire, fishing, shell ornaments use, language develop and others, have been associated to progressive increase of cranial volume and expression of diverse genes.

The *Homo sapiens* may be considered a eusocial species; the work is divided. A tendency to develop this type of behavior is inherited. Different environments have undergone changes in their exterior stimuli which their biological structure cannot be adequately adapted to given the limited period for that adaptation. The disease susceptibility including depression, may be a consequence of ancient human adaptations to a long-term stable environment [4]. A neurological background may be linked to genetic susceptibility to depression [5,6]. In postnatal stages the human is exposed to diverse experiences, and unlike to other primates, the human has ability to accumulate these experiences as memory [7]. The neuronal function remains a crucial factor for experience storing during the life. Neuroendocrine hormones triggered during stress may lead to diverse form of cerebral, endocrine and immune deregulation. Various types of substances are implicated in these functions and include epinephrine, norepinephrine, acetylcholine, substance P, vasoactive intestinal peptide, glucagon, insulin, cytokines, and growth factors. The stress response and induction of a deregulation in the cytokine balance can trigger diverse responses in the hypothalamic-pituitary-adrenal axis and sympathetic nervous system [8].

Distinct environmental and social triggers may be important in subsets of patients with depression tendency. Recently is important take into account the genetic mixing of human races. The races can also be modified without requiring migration, for instance, by religious or political influences [9].

Another change to be addressed is the competitiveness between individuals, as a biological fact. In primarily societies the groups competes for foods and in developed societies the human competes for reasons related with the work or social status. Various aspects of

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malfunction society or related to individual in terms of competitiveness, are kneed causes of depression.

Lesson Learned from Social Insect Studies (Concept of "Eusocial Species")

Pheromones play an important role in the physiological mechanisms underlying the development and maintenance of eusociality in insects. The queen pheromone system in social insects as the honey bee *Apis mellifera*, were found to produce a mixture of five compounds, three aliphatic and two aromatic, which have been found to control workers [10]. Mandibular gland extracts inhibit workers from constructing queen cells in which new queens are reared which can delay the hormonally based behavioral development of workers and can suppress ovarian development in workers. Both behavioral effects mediated by the nervous system often leading to recognition of queens (releaser) and physiological effects on the reproductive and endocrine system (primer) are attributed to the same pheromones. The animals respond according to the social needs of their hive. A debate focused on whether or not humans may be considered eusocial has been showed [11]. In Wilson's latest book, 2012's "The Social Conquest of the Earth", he refers to humans as a eusocial species. He supports his reasoning by stating our eusocial similarities to ants. Humans also fall under Wilson's original criteria of eusociality (division of labor, overlapping generations, and cooperative care of young including ones that are not their own). Through cooperation and teamwork, ants and humans gain a type of "superpower" that is unavailable to other social animals that have failed to make the leap from social to eusocial. Eusociality creates the "superorganism".

A hypothesis that could be raised at this point is whether the imprint that gives the pregnant mother to the fetus in its development determines individual changes in the eusocial context. Various forms of stress (e.g. social stress), determine both changes in the expression of receptors of various hormones or neurotransmitters and epigenetic changes [12,13], responsible for addressing social future of the individual, how do pheromones in eusocial insects.

Role of Prenatal Imprinting

Prenatal stress results in the hyperactivation of the maternal hypothalamo-pituitary-adrenal axis, leading to enhanced production of "stress hormones". Consequently, offspring exhibits elevated neuroendocrine responses to stress, including elevated secretions of corticotropin-releasing factor (CRF), adrenocorticotropin-releasing hormone (ACTH) and corticosterone [14], and a reduction in the density of corticosteroid receptors in the hippocampus [15]. Prenatal stress offspring shows from infancy to senescence and throughout adulthood marked memory deficits in numerous and particularly hippocampal-dependent, behavioral tasks [16,17]. Brain neurotransmitter systems changes with cognitive effects [18] and impact in the behavior of offspring also has been reported [19]. Epigenetic consequence in gabaergic interneurons from prenatal stress has been implicated in development of experimental schizophrenia [20].

A possible form of Depression Genesis based in the Imprinting from Prenatal Stage in the Human as Eusocial Species is Show

Starting from the premise that the human species evolved into a form of eusocial species, we might consider a hypothesis about the origin of certain forms of depression. Various mechanisms of evolutionary adaptation have led to the structuring of eusocial species that meet the

following three criteria: cooperative brood care (including brood care of offspring from other individuals), overlapping generations within a colony of adults, and a division of labour into reproductive and non-reproductive groups [21]. These criteria were used to classify different insects and small mammals like eusocials. But the human species is included by some authors as a kind of eusocial species, since meets these criteria. In eusocial insects, organic drastic changes occur as a result of pheromones action, as is the condition of the individual to move from state to infertility or fertility, or vice versa, as response to punctual needs of the community. The queen releases pheromones that cause these changes.

Is feasible to say that individuals of the human species may have a "personality", based on the social needs of the maternal in pregnant time?

In human primitive societies a struggle between individuals for primary survival as the food consecution may be presented. In these forms of human society that develop in groups or gangs, and given its status as warrior, its individuals generally have a short life due to its high mortality from death in "battle". Youth must be reproduced in bulk, very early in the time of development of their fertility. In Colombia we have seen frequently pregnant girls even before menarche. These young pregnant women are part of a warrior society, are active as their own acts of the struggle for life between gangs. This permanent stress during pregnancy may imprinting drastically their offspring's brain, almost certainly in the hippocampus. This issue is scheduled to serve in this complex community as a warrior, and quickly in its infancy acquires these characteristics, with the development of a typical warrior personality. These individual not has fear and pain sensitivity. We can assume that these guys may have less sensitivity to steroid hormones or pressure amines (perhaps mediated reduction of hippocampal receptors) and epigenetic effects that modify their personality. Already in a broad social context, we might consider these conditions as a way for generating a criminal personality. Such individuals may be modified if are remove of social medium, but difficulties are large, among other because developing depression. This raises a mismatch between social programming individual imprint left by the mother, and the new social reality that he faced.

Across society an individual with multiple benefits during prenatal development: adequate food supply, low stress, low release of catecholamine and steroids by the mother. We could say that this individual has greater sensitivity to external stimuli, including social type stimuli and would be less risk of developing a sociopathic personality. If this individual is exposed to a hostile environment as a warrior society (in Colombia is common the illegal recruitment of children for integration into criminal gangs), ensue form of depression that arises here. A social programming that is thwarted by factors outside the individual.

Conclusion

A form of depression based in the discordance between maternal prenatal imprinting and social outcome of individual has been hypothesized. An individual programming as response to social needs, can cause organic depression, if the individual is confronted with another kind of society for which was not designed.

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