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RESEARCH ARTICLE

What Are We Like: Is It a Matter of Genetic Inheritance or Not? A Narrative Review

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Abstract

Background. Scientific literature in psychology considers personality as an organization of ways of being, knowing, and acting that ensures unity, coherence, and continuity, stability, and planning of the individual's relations with the world.

Personality is the outcome of two distinct constructs: Temperament and Character. So, personality is the result of the interaction between biological aspects (Temperament) and experiences of everyone in life, interacting with the environment[1].

Scientific literature now largely agrees that adversity in the early years of life has broad long-term consequences on the neuroendocrine, immune, and metabolic systems[2] as well as on neuroplasticity and neuronal morphology.

Here we analyze the hypothesis that maternal environmental factors (air and chemical pollutants, maternal health, eating behaviors, maternal and fetal stresses, caregivers' behaviors, etc.) can cause epigenetic alterations in the offspring during the prenatal that shape the trait's personality of the offspring themselves and that partially influence their.

Methods. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used to develop this systematic review. PubMed, Scopus, PsycINFO, and Biosis databases were searched for primary research articles published between 2010 and 2023 looking for English language articles containing the term "prenatal" and any of the following terms: "anxiety", "brain development", "depression", "gestation", "maternal health", "maternal stress", "mental health", "newborn health", "perinatal programming", "pregnancy", "prenatal stress", "resilience to stress", "transgenerational epigenetic inheritance", "personality", "personality trait", "environmental epigenetics". Relevant papers evaluating the relationship between maternal environmental factors and the personality traits of the offspring were subjected to a more thorough evaluation.

Results, and Conclusions. Among the 111 studies identified, only 3 met the primary question. There is evidence to support the hypothesis of correlations between environmental exposure during the intrauterine fetal period and

personality traits of the newborn.

Limits: Multiple limitations were found based on the lack of research on this specific topic, although such a field of research can be important for developing effective strategies for primary prevention.

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1. Introduction

Scientific literature in psychology considers personality as an organization of ways of being, knowing, and acting that ensures unity, coherence, and continuity, stability, and planning of the individual's relations with the world (Caprara & Gennaro, 1994).

Personality is the outcome of two distinct constructs: Temperament and Character. So, personality is the result of the interaction between biological aspects (Temperament) and experiences of everyone in life, interacting with the environment[1].

Other authors have named this biological, genetic, and time-stable basis as a personality trait[3].

This work aims to understand whether the Personality trait is due only to genetic inheritance, and therefore to Chance, as well as the meeting of maternal and paternal alleles, for each chromosomal locus, at the moment of conception, or if it is shaped by something else.

Scientific literature now largely agrees that adversity in the early years of life has broad long-term consequences on the neuroendocrine, immune, and metabolic systems[2] as well as on neuroplasticity and neuronal morphology.

In the scientific literature, there is a precise line of investigation on the origin and development of diseases deriving from the exposure of the fetus, directly or indirectly through the mother, to certain environmental factors[4][5][6].

This work is based on the hypothesis that the perinatal environment can have an impact on the health of the fetus and its subsequent life.

Lapehn notes[7] that the placenta is uniquely positioned to evaluate prenatal exposures from this environmental influence perspective (where "environment" encompasses physicochemical, behavioral, socioeconomic, etc. factors). In fact it is an ephemeral and essential fetal organ that manages the transport of oxygen, nutrients, waste, and endocrine signals between the mother and her unborn child.

As Liester & Sullivan[8] recall, the interactions between individuals and their environment that affect the normal development and functioning of the human brain are mediated by changes in DNA, known as epigenetic changes.

In addition, in the last six years studies on placental epigenomics have been carried out to obtain biological information on any placental alterations related to the perinatal period of unborn babies, including preterm birth, intrauterine

underdevelopment, birth weight and/or size[7].

According to Nakamura et al.[9], the placenta epigenome can be considered a biochemical record of the prenatal environment and a potential mechanism of its association with future fetal health. His study provides the first evidence of associations between placental DNA methylation and the baby's behavioral and emotional difficulties.

2. Epigenetics

British biologist Conrad Waddington[10] proposed the term epigenetics almost a century ago to describe the molecular events involved in early embryonic development.

Subsequently, this term was adopted by many researchers to describe all developmental events that begin with the fertilized zygote and end with the mature organism[11].

Under the "umbrella" of the term epigenetics, all the processes that were not easily interpretable in genetic terms, but which, due to their peculiarity of being transmitted between mother and child, have a hereditary component, have been grouped over time[12].

As knowledge has advanced, it has been realized that epigenetic changes provide a mechanism for the transmission of information not encoded in DNA. Such information includes a historical record of interactions between the environment and the genome, which is stored as a form of cellular memory (Liester, 2019)

Given the heterogeneity of the processes encompassed in the term epigenetics, Liester's definition—"the study of changes in gene expression that do not result from alterations in the DNA sequence"—has been considered here.[8].

2.1. Epigenetic processes

Epigenetic changes that can lead to gene variations downstream of the process can occur through chemical, structural, and positional changes in chromatin, resulting in the activation or deactivation of genes. These mutations are stable and can be reversible or, sometimes, persistent even across multiple generations.

Transmission of epigenetic information to subsequent generations can occur through fetal programming, behavioral intervention, or germline transmission[13].

Four of the most frequently analyzed are briefly mentioned here.

2.1.1. DNA methylation

DNA methylation is the direct addition of a methyl group to a DNA base. This process occurs in the majority of cases on cytosines adjacent to guanine residues. DNA methylation, within the promoter region of a gene, results in gene silencing through the recruitment of repressors and the inhibition of transcription factors (Jones, 2012).

It is widely believed that the covalent binding of methyl groups to DNA is an important regulator of gene expression[14][15].

2.1.2. Histone changes

To protect the DNA in the nucleus of the cell and guide the transcription process, it is wrapped around basic chromatin "packaging" proteins (histones, "epigenetic marks") that can undergo post-translational modifications[16][17]. Acetyl and methyl modifications, along with phosphorylation, are the most frequent types of histone modifications. Depending on the number and location of the marks on the histone complex, they determine the activation or deactivation of genes[17].

2.1.3. Non-coding RNA

Non-coding RNAs (ncRNAs) can intervene in the epigenetic process by mediating various intracellular processes[18]. An ncRNA is a functional RNA molecule transcribed from DNA but not translated into protein. There are also long non-coding RNAs (lncRNAs), another subgroup of RNAs longer than 200 nucleotides that have the function of remodeling chromatin and constitute transcriptional and post-transcriptional regulators[19].

2.1.4. Chromatin localization near the nuclear envelope

The location of chromatin within the nucleus influences gene transcription[20]. For example, chromatin next to the nuclear lamina lining the inside of the nucleus envelope is generally associated with gene repression, while the placement of the same chromatin away from the lamina is associated with gene activation[21][22].

3. Factors that can trigger epigenetic mutations

Epigenetic processes modulate interactions between individuals and the environment, and a wide range of environmental factors can trigger epigenetic modifications. These factors include pollutants and toxins[23][24], alcohol[25], addictive substances[26], eating behaviors[27], activity and exercise[28], exposure during gestation to maternal nutritional factors[19], and stressors or traumatic episodes experienced by the mother[29].

All of these factors can produce epigenetic changes that affect, even permanently, neuronal development, neuroplasticity, cognition, and behavior even permanently[30][31]. In fact, for example, races of peculiar and different epigenetic modifications have been found, 60 years after exposure, in individuals who in the fetal period were exposed to famine during the Dutch famine in winter 1944[32].

4. Transmission of epigenetic mutations

Epigenetic changes can be passed down through generations, a process called transgenerational epigenetic inheritance[33]. Transgenerational epigenetic inheritance involves the transmission of non-genetic information from parent to offspring through germ cells. Such information has been shown to persist for 14 generations[34]. Other evidence of the

transmission of transgenerational epigenetic modifications has been provided in studies of the descendants of Jewish survivors of the Holocaust[35], where data emerged that adult children of those who experienced that tragedy showed lower methylation of site 6 of the FK506 binding protein 5 (FKBP5) compared to the control group.[36][37][38]. Epigenetic and behavioral transmissions from mother to offspring have also been demonstrated regarding dopamine and its transporter DAT[39].

5. Effects on the fetus and on the first moments of life resulting from certain environmental conditions in the intrauterine and/or perinatal period

In the analysis of some perinatal stressful conditions, Lehnig[40] notes that preterm infants can face multiple challenges both in the intrauterine and immediate postnatal periods.

According to Zitkovsky[41], premature infants lose a) the protection of the placenta prematurely, b) the element that modulates homeostasis in the intrauterine environment, and c) protection from events that can have epigenetic and potentially harmful effects on neurological development in newborns.

In addition, the mother of the preterm infant, due to the premature birth and the difficulties that arise from such an event, may experience a high rate of MCM (Maternal Childhood Maltreatment). This can generally be summarized as maternal (including physical abuse, emotional abuse, i.e. related to maternal responses that are not in tune with the needs of the offspring), physical or emotional abandonment (according to attachment theory), or even sexual abuse[42][40].

An observational and longitudinal research study, called CANDLE (acronym for Conditions that Affect Neurocognitive Development and Learning in Early Childhood) has carried out by the University of Tennessee. This study aimed at identifying the factors that affect the development and learning ability of the child during the mother's pregnancy. It has been shown that maternal urinary concentrations of 21 phthalate metabolites sampled during the second and third trimesters of pregnancy were present in the placental transcriptome and therefore in contact with the nutrients and vital environment of the fetus[43][44][45][7]

It is therefore almost universally recognized that the developing fetus is influenced by multiple aspects of the environment in which the mother lives, what she is exposed to, and her mental health[46][47].

Adversity in early childhood has also been associated with a decrease in hippocampal volume, and the hippocampus is most likely the area of the brain most affected by stress in the early years of life[48]. This taking into account the developmental times of the individual brain structures potentially involved: the human hippocampus is not fully developed before the age of 2, while the frontal cortex matures mainly between the ages of 8 and 14, and the amygdala continues to develop until early adulthood[49]. The sensitivity of the hippocampus to the "injuries" experienced in the very first period of life is therefore particularly important, as this subcortical structure plays a key inhibitory role in PVN (paraventricular nucleus) activation of the HPA axis (hypothalamic-pituitary-adrenal)[40].

5.1. Hypothalamic-pituitary-adrenal (HPA) axis

Numerous studies address the hypothesis that maternal exposure to trauma, via the release of placental corticotropin (pCRH), can result in intergenerational transmission that begins during intrauterine life[50].

There are elements in the external environment that induce permanent changes in the stress response of the HPA axis and glucocorticoid levels, and the most important factor is adversity in the early life period[51].

Glucocorticoids activate the transcription of genes associated with glucose and lipid regulatory pathways and thus control both physiological and pathophysiological systemic energy homeostasis[51].

Both animal and human data have emphasized permanent and potentially deleterious neuroendocrine effects of stress exposure during early childhood or child development[52][53][54][55].

Dysregulation of cortisol and deficient regulation of glucocorticoid feedback have been identified as biological correlates of depression and anxiety disorders in adults[56][57][58].

A large clinical literature has characterized major depressive disorder (MDD) as a condition associated with excessive basal cortisol secretion and inadequate regulation of the inhibitory feedback of the constituents of the hypothalamic-pituitary-adrenal (HPA) axis[59].

5.2. Mitochondrial changes

Mitochondrial changes can also be combined with epigenetic processes.

It is now clear that mitochondria can adapt morphologically, driven by the presence or absence of environmental stress, and that such dynamic adaptations are mediated by specific mitochondrial functions[60][61][62]. Chronic stress can alter mitochondrial dynamics in the brain both directly through the action of stress hormone receptors and indirectly through alterations of the neuroendocrine axis[63][64][65].

Mitochondrial function/dysfunction may play an important role in the link between prenatal and/or postnatal stress and neurodevelopmental outcomes in infants[66].

In addition, it should be noted that some perturbations in mitochondrial dynamics have been identified in numerous neurodegenerative conditions (e.g., Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis)[62], and neurodevelopmental conditions such as autism spectrum disorder[67][2].

6. Discussion: Correlation with Environment and Personality Trait

As highlighted so far, numerous studies show the correlation between maternal environment and development of pathologies in offspring, whether they manifest at the time of birth or later in life (even after a few decades), or whether they are transmitted to subsequent generations.

There is therefore a considerable body of scientific work that testifies to the effects of adversity on mothers and offspring during the prenatal period[68][69][70][71][72]. In particular, such "insults" have been associated with increased responses of the Hypothalamic-pituitary-adrenal (HPA) axis and more generally with autonomic responses to stressors[73][74][75][76].

Last but not least, the work of Heim & Nemeroff[53] shows that studies that have evaluated parental neglect and abusive behavior towards children during the first weeks of life have found lower stress management skills, less independence, and higher levels of anxiety and stress. This resulted in increased activity in the HPA axis and central nervous system when the same individuals were subjected to stressors in later life[53][77]. This is because in post-traumatic stress disorder ACTH responses are attenuated and lead to reduced cortisol secretion and altered negative feedback to the hypothalamus[78].

On the other hand, there is little research that correlates factors of the maternal environment to the psychological, non-pathological profile of the offspring, and in particular, to their character traits.

We could deduce some information in this regard by carrying out an operation, so to speak, "negative" or "backward," from studies that relate placental and/or perinatal "insults" with the early onset of psychological distress such as anxiety disorders or otherwise "unexplained" PTSD in the child in the first months of life. This is because, beyond the consideration that each case has its peculiarities and uniqueness, psychological disorders such as anxiety or depressive disorders may be more present in subjects with personality traits that have a greater component of introversion, according to the Big Five theory[79]. Some researchers have tried to answer the question that arises spontaneously from empirical observation deriving from clinical activity: "Why is it that even though many people experience trauma, only a minority of them develop a persistent disorder such as post-traumatic stress disorder?"

Tronick & Hunter[80] observes how the development, the quality of an individual's functioning, and therefore his or her permanent character characteristics (personality traits), are also the result of repeated experiences and processes that the child considers or may consider traumatic.

It should be remembered, for example, that the meaning given by children to the game of being lifted or thrown into the air by a parent can lead to fun and excitement in some and fear and despair in others.

These behavioral and meaning-attribution differences may be related to Temperament or modulation of one's limbic structures[80]. In other words, if a child has a low threshold of amygdala reactivity, he or she may experience as traumatic an event that another person of the same age considers neutral or even pleasant[81].

The difference in attribution pointed out by Tronik Hunter[80] and different character predispositions resulting from different thresholds of reactivity/functioning of limbic structures highlighted by Porges[81] explain the empirical finding that, although most of us may be exposed to a traumatic event in our lifetime, only a minority will develop a persistent disorder such as post-traumatic stress disorder[82].

Currently, only two of the studies reviewed explicitly address the topic.

In the first, Davis et al.[83] suggest that the exposure of fetus to placental corticotropin, whose presence increases in the third trimester of gestation and which, the author points out, is of placental origin and not hypothalamic, influences the infant's Temperament. These authors found that fetuses exposed to lower levels of maternal CRH at 25 weeks of gestation were rated by their mothers as having the least fear and distress behaviors during childhood. Moreover, they point out that the 25th week is the most sensitive period to observe the influences of CRH programming on infant Temperament[83].

In the second work, Moog et al.[50] underline that the intergenerational transmission of the effects of maternal exposure to trauma, even if experienced in childhood, can occur in the postnatal life of the child through maternal psychological states related to the stressful event he experienced in childhood, on the dyadic mother-child relationship, and suboptimal parental behaviors[84][85].

Moreover, Moog shows that the traumatic childhood exposures of the future mother also have an impact on the development of the fetus since the presence of pCRH (placental corticotropin) is a predictor of infant Temperament[50].

Even more interesting, is what Barker & Osmond[86] have shown about the fetus' ability to generate "predictions" about the nature (in terms of pleasantness/unpleasantness, affect/hostility) of the extrauterine world, and such "predictions," which Tronik defines as the results of neurosomatic embodied systems[80], influence and can characterize how the fetus before, and the newborn then, acts in the world[87].

These "predictions" are, in other words, "contents," and "meanings" with no awareness implications, devoid of timestamps, narratives, and images[80].

According to Tronik's thought above, the newborn, even the premature one, Montirosso hypothesizes[88][89][90], can experience a state of motivated and embodied discomfort, perhaps even an emotional state of fear, or a state of pleasure that guides his behaviors in the world. Although in different terms, Tronik[80] adds that the emotional state of fear described by Montirosso results in a predisposition to introversion, and that of pleasure leads to a predisposition to extroversion.

6.1. Limitation of Current State of Scientific Knowledge

Ethical and practical difficulties hinder the researchers from conducting the clinical trial in infants. There is too little research on the correlation between environmental exposure during the intrauterine fetal period and the personality traits of the newborn. The lack of studies on this topic will need to be addressed in future studies.

7. Conclusions

In literature, there is a strong background on which the hypothesis of correlations between environmental exposure during the intrauterine fetal period and the personality traits of the newborn is based. Despite this, there is an almost total absence of studies on this specific topic, although such a field of research can be important for developing effective

strategies for primary prevention. In fact, the quality of the mother-infant relationship is or can be influenced by the characteristics of the newborn (e.g., Temperament) from the moment of birth or even before. Knowing the dynamics of its genesis would give us the possibility to intervene before any damage arises.

Statements and Declarations

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