

Early Programming during Attachment Development and its Relevance for Risk/Resilience of Neuropsychiatric and Cardiometabolic Diseases during Adulthood

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Abstract

Social and cultural environmental factors influence the development of susceptibility to diseases in adulthood since the peri-natal stages of life. Sociotype describes the way in which interactions between social, cultural and environmental factors influence health. It plays a role as important as that of the genotype and phenotype in the balance of the health/disease processes during all the life span. Attachment forms part of the sociotype and is defined as the innate biological system that characterizes the link between an infant and a bonding figure. It increases the possibility of survival to a reproductive age and determines empathy and intimacy that when incorrectly established may be the cause of a number of pathological conditions in the adult life. Different types of attachment have, as a consequence, physiological and endocrinological alterations that result from the exposure to stressful and/or traumatic events during early stages of life. These constitute long- term plastic changes in structures in the central nervous system that produce in alterations in signaling molecule production that may arise from epigenetic cues established during the early stages of life in trauma- exposed subjects and that may lead to increased risk of diseases in adulthood. Therefore, sociotype and attachment might determine epigenetic alterations that may act on biological pathways involved in the comorbidity of cardiometabolic and neuropsychiatric diseases.

Keywords: Epigenetics; Attachment; Neuropsychiatric disorders; Cardiometabolic disorder

1. Introduction

Sociotype determines the influence between social, cultural and environmental factors and health. It acts together with the genotype and phenotype [1]. Attachment, which is the innate biological system that characterized the nature of the interaction between an infant and a bonding figure, forms part of the sociotype. Sociotype also takes into account cultural, environmental factors [2]. Correct attachment elevates survival to a reproductive age and helps establish empathy and intimacy. Attachment disorders may underlie a number of neuropsychiatric and cardiometabolic disorders in adult life [2-5]. There are physiological and endocrinological differences in brain functioning in response to the type of attachment that is established during infancy and which are the result of the exposure to significant events that happened during early stages of life [6]. Modifications produced in brain structures and in the amount of neuroactive substances released by the brain could be of long duration [7] and may be epigenetically determined leading to the risk (or resilience) to develop cardiometabolic and neuropsychiatric diseases in the adult [8-10]. Thus, sociotype and attachment might influence the comorbidity of these complex diseases [3, 8, 9]. In this paper we analyze the proposed relation between attachment and possible changes in brain structures and the differences in the release of different neuroactive substances that may be epigenetically determined and that may be involved in the comorbidity of neuropsychiatric and cardiometabolic diseases.

2. Early Programming by the Genotype, Phenotype and Sociotype

The term "sociotype" has recently been coined to describe interactions between social, cultural and environmental influences and their consequences on the health/disease process. Nowadays, susceptibility to chronic disease is being considered as the result of disharmonic interactions between the genotype, phenotype and sociotype. Social neurosciences (NS) and developmental NS have been acting as key tools to the knowledge of the participation of the sociotype on disease development [1]. The influence of the "genotype" and "phenotype" during the peri-natal stages of life upon the development of susceptibility to diseases in adulthood has been widely studied in the last years. However, the way by which social and cultural environmental factors influence susceptibility to diseases has been less studied. The social and cultural environments determine growth, development and life-long behavior of a human, including relationships, lifestyle and coping strategies since early stages of life and although they have been related predominantly to neuropsychiatric disorders they have almost not been included as important determinants of susceptibility to other complex diseases including cardiometabolic illnesses [1].

Attachment theory is included in the sociotype and plays an important role in development of empathy. Attachment between the parent and the child, which is importantly related to empathy is established during the first years of life in humans and may leave epigenetic prints that could alter the risk (or resilience) to develop neuropsychiatric and/or cardiometabolic diseases during adulthood. The plasticity in neuroanatomic structures [8, 9] and in the release of neuromediators [8, 9] that participate in attachment have been linked to epigenetic mechanisms. Recent studies support the theory that insecure attachment is a risk factor for the development of disease and chronic illness, particularly for conditions involving the cardiovascular system [3]. Alteration in components of the sociotype such as poverty and poor education favor the presentation of cardiometabolic and mental disorders and contribute to

susceptibility for non-communicable diseases. Sociotype modulates the genotype expression and thus the phenotype through epigenetic cues [1].

The sociotype is determined by at least three domains [1]:

- The health domain which includes life experiences, beginning with attachment, empathy and imprinting. It determines personality development as a whole, and the appearance of specific personality traits such as a sense of humor. The experiences belonging to the health domain develop slowly in human's maturation and are established during the period of infancy, childhood dependency, and adolescence. Secure or insecure infantile and childhood parental attachment programs reproductive strategies. The health domain determines very relevant activities to individual equilibrium such as sleeping, sexuality, and eating which occupy more than one third of a person's life.
- The domain of relationships which considers the relation to family, peer group and friends, lovers, and people in authority. Partner selection determines the genotype and phenotype of the next generation. Nevertheless, how much of this domain is biologically or psychologically driven has not been determined and goes beyond the aims of this paper.
- The environment domain which includes education, employment, economic circumstances, and time spent at work, home, and during leisure activities. It also includes political, ideological, and societal values which may also influence cardiometabolic and neurobehavioral health.

Other factors that have a significant influence on health behaviors are social networks, media, and the information technology revolution. Religiosity affects all domains and provides a meaning to one's situation as well as communal support. Some individuals find an intellectual way to face such needs through humanism and altruism [1]

3. Social Neuroscience and Developmental Social Neuroscience

The investigation of neural, hormonal, cellular, and genetic mechanisms that underlie social structures, processes, and behavior is the field of study of social neuroscience. Social sciences also studies mechanisms of other mental function issues such as social decision making [11, 12], morality [13, 14], reputation [15], [16, 17] and addresses the influences between social and biological levels of organization [18]. These mechanisms impact aspects of the social life including education, health or public policy [18, 19].

Noninvasive functional neuro-imaging techniques are an important tool for social sciences since they allow for the localization of areas with neural activity while individuals perceive and respond to particular social stimuli thus providing insights on how the social mind develops and on the functioning of several socioemotional, cognitive processes and moral reasoning [4, 20-24], including facial emotion processing [25], social perspective-taking [26], social exclusion [27], ostracism [28], emotion regulation [29], and empathy [17].

4. Attachment Theory

The human being struggles in life between a wish of being alone, autonomous, and free or being close to other members of its specie, and at least partially under the control of others. Human infants are biologically programmed to look forward to be attached to others and seek to sustain attachment. Attachment is based on a highly conserved set of behaviors that is present in humans and many other primate species [30]. Attachment is defined as an innate biological system that promotes a search for proximity between an infant and a bonding figure. It increases the possibility of survival to a reproductive age [31]. Attachment theory draws insights and emerges from principles of psychoanalysis, evolutionary biology, cognitive-developmental psychology, ethology, physiology and control systems theory [32]. Attachment security provides is the basis for empathic concern, caregiving and forgiveness.

Sigmund Freud in 1914 [33, 34] noted that mother-infant attachment has critical importance and suggested that aberrant experiences were the cause neuroses in adults. However, it was the psychiatrist John Bowlby who integrated our current view of the mother-infant relationship contributing to the formulation of the Attachment Theory. Bowlby carefully observed the interpersonal relations between newborns and the primary caregivers and suggested that this relationship model is a result of evolutionary pressures to facilitate the infant's survival when facing a potential predator or other living creatures or when being exposed to other dangerous situation [35]. One of the most important premises of this theory is that the newborn is in need of developing a relation with at least one primary caregiver to succeed in his social and/or emotional development and, mainly, for learning to regulate emotions. When the emotional link between the caregiver and the newborn is successful, the infant develops a secure platform to explore the surrounding environment and the world, becoming a secure adult and learning to regulate emotions when placed in risky or favorable situations. Thus, the sense of safety of the child was provided by the caregiver's protection and the cause of the proximity-seeking behavior of the child. Bowlby postulated that adaptation is the product of both developmental history and current circumstances (never either alone) [35-37]. Furthermore, pathology is never caused only by the early experience, but it has a special significance due to the nature of development. Developmental history forms part of current context, participating in selection, engagement, and interpretation of experience and in the use of available environmental supports. According to Bowlby, the child's attachment is built during the first year of life simultaneously to the formation of a mental model of the self and of others by the child and is based on its earliest relationship to the protection providing figure [37]. Although the brain is imprinted by the earliest attachment relationships, it continues to be sculpted during adulthood and can be markedly influenced by relationships during one's lifespan [38].

The work by developmental psychologist Mary Ainsworth was incorporated to the attachment theory. In the 1960s or 70s, she described the results from experiments in which babies were exposed to strange situations, observing and classifying the main attachment patterns that are developed between caregivers and newborns [39, 40]. Table 1 summarizes the different attachment patterns.

Secure Attachment	<p>The caregiver functions as a secure base for exploration.</p> <p>The child protests the departure of the caregiver and seeks proximity and is comforted when this occurs, allowing him or her to explore the surroundings again.</p> <p>The baby may be comforted by strangers but shows a clear preference for the caregiver.</p> <p>The caregiver reacts appropriately, quickly and consistently to the needs.</p> <p>A safe parental bond with the child is successfully formed.</p>
Anxious Attachment	<p>The newborn is unable to cope with the caregiver's absences and does not stop crying when the caregiver is trying to comfort him. The newborn looks for guarantees that the caregiver is there constantly.</p> <p>The caregiver is excessively protective of the child.</p> <p>The caregiver does not allow the existence of risks or that the child takes a step towards independence.</p>
Ambivalent or resistant Attachment	<p>The caregiver does not function as a secure base, the baby seeks proximity before the separation occurs.</p> <p>The child is intensely irritated in the face of separation allowing ambivalence, anger, reluctance to embrace the caregiver, and then he resumes play again.</p> <p>The baby is seeking the availability of the caregiver, looks for the contact, but resists furiously when it is attended by the caregiver.</p> <p>The child cannot easily be comforted by strangers.</p> <p>The child always feels anxious because the caregiver's availability is never consistent.</p> <p>The caregiver often shows inconsistency between the appropriate and negligent responses.</p> <p>In general, the caregiver only reacts when there is an increase in the anxious behavior or anguish of the newborn.</p>
Avoidant Attachment	<p>There is little affective interchange in the game between the child and the caregiver.</p> <p>The child does not seek the approval of the caregiver.</p> <p>The child shows little or no irritation with the departure of the caregiver. There is no visible response to the return of the caregiver, ignoring or moving away from him without there being any effort to maintain contact.</p> <p>The child treats any stranger in a similar way to the caregiver.</p> <p>The child feels that there is no attachment, therefore, he is rebellious and develops low self-esteem.</p> <p>The caregiver shows little or no response to the irritation of the child.</p> <p>The caregiver discourages crying and encourages the baby's independence.</p>
Disorganized Attachment	<p>Some stereotyped behaviors in the child are shown, such as hugging oneself or constant swaying.</p> <p>There is a lack of a coherent strategy of attachment in the child, which is shown through contradictory behaviors such as approaching the caregiver, but with the face upside down</p>

	<p>and without establishing eye contact.</p> <p>The caregiver may be scared or inflict fear, be intrusive in the game or exploration of the child, withdraw without notice, have a negative attitude, confusion of roles, emotional communication errors and abuse.</p> <p>This type of attachment is often associated with many forms of child abuse.</p>
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Table 1: Attachment patterns developed between the caregivers and the newborns.

5. Anatomy and Molecular Substrates of Attachment

An important field of study in attachment is the physiological and endocrinological consequences of the exposure to stressful and/or traumatic events during early stages of life. It is a bidirectional process defining the infant's cognitive and emotional development [41]. It is well known nowadays, that subjects that have been exposed to constant trauma from infancy or during adolescence show elevated levels of cortisol which leads to a flat or abnormal response against new adversities known as learned helplessness [42]. The model of learned helplessness explains a great deal of the fact that individuals who have already experienced adverse events in the past, reproduce a model of life in which there are more dangerous or adverse events than in the general population [7, 43]. Moreover, long term changes in the central nervous system in subjects exposed to trauma show a decreased volume in the hypothalamus and emotional association areas in the brain [6].

5.1. Anatomical structures participating in attachment in parents and infants

Attachment formation includes a maternal behavioral system to provide care and an infant behavioral system that determines the seeking for parental care being thus a reciprocal attachment. It programs the infant's emotional and cognitive development and helps in the maturation of the developing brain [17]. Importantly, most of the structures involved in attachment have also been found in susceptibility for the comorbidity of neuropsychiatric and cardiometabolic diseases [8, 9].

5.1.1. In the child: The amygdala has been proposed to be determinant to the affective and motivational behaviors. However, the amygdala is not activated during social interactions with the primary caregiver in infancy nor during encounters with aversive stimuli. Thus, it has been postulated that the amygdala may not be associated with early life infant attachment but is involved in social behavior in adulthood [44, 45]. Nevertheless, the lack of plasticity in the infant amygdala seems to participate in fear learning in adults and in the aggressive response to social provocation.

The maturation of the prefrontal cortex and its reciprocal connection with the limbic system are necessary for empathy and a development of a sense of self to account for more complex forms of cognitive abilities such as mentalizing, intersubjectivity and motivation to care for others [17]. The prefrontal cortex plays a restrictive role in

the release of spontaneous or recently acquired (i.e., learned) behaviors [46, 47]. The orbitofrontal cortex is thought to be a self-regulatory region that inhibits aggressive impulses [48].

5.1.2. In the parent: Empathy needed for parenting depends on large numbers of brain structures and systems that include structures of the limbic cortex and neocortex such as the amygdala, insula, anterior cingulate cortex and orbitofrontal cortex. Hypothalamic–midbrain–limbic–paralimbic–cortical connections collaborate to make possible the parent response to infants. They participate in emotion, attention, motivation, empathy, decision-making and other mental capacities needed for parenting [49]. Efferent circuits from the medial preoptic area of the hypothalamus regulate the consummatory and appetitive aspects of maternal behavior. In contrast, an amygdala–hypothalamus circuit depresses maternal behavior by activating an aversion system [50]. There is a marked reduction in activation and amygdala–midbrain connectivity in males receiving oxytocin that suggests an important role of this neuropeptide on the structure reactivity and brainstem interactions in humans indicating the possibility of a neural mechanism for its effects in social cognition [51].

Parenting also requires of the participation of the autonomic nervous system, hypothalamic-hypophysis-adrenal axis, and endocrine systems that regulate bodily states, emotion and reactivity and of the reward, social attachment, and aversion systems [18].

In mothers with secure attachment there is activation of oxytocinergic and dopamine associated reward processing regions of mesocorticolimbic brain regions such as the ventral striatum when they are aware of their infant’s smiling and crying face. In contrast, in insecure mothers, there is increased insular activation when they observe sad faces of the infant [52].

5.2 Mediators in parenting behavior and infant attachment behavior

5.2.1 Neuropeptides: Neuropeptides and their receptors play an important role in regulating social behaviors, including attachment, social recognition and aggression [53-58], particularly oxytocin [58] and vasopressin which have been called “social neuropeptides” and opioids. Oxytocin and vasopressin have also been found to participate in susceptibility to comorbid cardiometabolic and neuropsychiatric disorders [8]. Steroid hormones have a sex specific effect on animal social behavior [59-61], modulating social behavior.

5.2.1.1. Oxytocin: Oxytocin facilitates maternal behavior and increases pro-social behavior in humans [61], social cognition and empathy. Oxytocin modulates many behaviors in mammals, and humans, such as aggression, affiliation or social memory [11, 62, 63]. Intranasal administration of oxytocin improves memory to help recognize faces, but not for non-social objects [64].

Oxytocin inhibits the natural avoidance of proximity and defensive behavior, thus facilitating approach behavior [65]. Although it facilitates trust, it also elevates the disposition to accept social risks in experimental animals [66,

67]. However, this does not happen in humans [68]. Oxytocin promotes a better communication behavior during conflict in couple discussion and significantly reduced salivary cortisol levels after the conflict [69]. Furthermore, oxytocin is also a key element in social motivation [70], altruism [71] and cooperation within groups [72]. Finally, a role for this neuropeptide in dishonesty helping a group has also been observed and might underlie a functional approach to morality [73].

Many brain structures act as targets for oxytocin including the hypothalamus, amygdala, hippocampus, brainstem, heart, uterus, and regions of the spinal cord that regulate the autonomic nervous system, especially the parasympathetic branch [73]. The activity in the hypothalamus- hypophysis-adrenal axis is reduced by oxytocin and social interactions [64]. Secretion of hormones of this axis such as cortisol, corticosterone or adrenocorticotropic hormones is the consequence of separation from the attachment figure. Moreover, hypothalamus- hypophysis-adrenal axis activity descends when there is a reencounter of the parent and child. Oxytocin also seems to promote the benefic effect of social support during stress responsiveness [74]. The interaction between oxytocin and dopamine promotes a sensation of reward during social encounters; it enhances the motivation to engage in social interactions, increasing the probability of approach and decreasing withdrawal [75].

A naturally occurring genetic variation of the oxytocin receptor is related to both empathy and stress profiles. This was discovered in a study in which a polymorphism (rs53576) of the oxytocin receptor was tested in association with empathy and stress reactivity [76].

5.2.1.2. Vasopressin: Vasopressin participates in maternal behavior [77, 78]. It also plays an important role in intermale aggression in rodents [79, 80] by either increasing or diminishing aggression depending on the brain region into which it is liberated. However, differences in the functioning of this mediator may differ in humans and other species since extrapolating behavioral, neurobiological and molecular mechanisms of aggression within species is difficult [81].

There is a marked sexual dimorphism in the responses to intranasal vasopressin inducing agonistic and/or antagonistic responses toward faces of the same-sex in men and women according to the sex of the subject being tested [82, 83]. Intranasal vasopressin administration also enhances the presence of giving a significance to facial expressions that express emotions [84] and the perception of sexual stimuli in human males [85].

5.2.2. Steroid sexual hormones: Hormonal events of late pregnancy including the rising of estrogen and prolactin levels and declining progesterone levels, act on brain mechanisms to either decrease fear/aversion of infant-related stimuli or increase attraction/approach toward infant-related stimuli [49]. Testosterone has also been associated to affiliative behavior, stress response and social aggression. Testosterone might act through the reduction of the activity in the medial orbitofrontal cortex [86]. The results suggesting that elevated testosterone levels are positively associated with aggressive are controversial [48]. Although it increases aggressive behavior in animals, fluctuations

in testosterone levels induced by situations do not seem to be relevant to human aggression [88]. Sublingual administration of testosterone in women caused a substantial increase in fair bargaining behavior, thereby reducing bargaining conflicts and increasing the efficiency of social interactions. However, in males, the beliefs about the effects of testosterone generating unfair behavior [89] and therefore the belief that testosterone is present or has been administered might cause expectations of aggressive behavior, rather than inducing an actual increase in aggressiveness [90]. In males, testosterone might generate a more general range of motivated behaviors, associated to dominance behavior including the motivation to achieve or maintain a high social status [48].

5.2.3. Opioids: Endogenous opioids influence social bonding and affiliative behavior. They mediate the rewarding effects of social affiliation. Opioids are released during social contact and this release is rewarding [90, 92].

6. Attachment and Sociotype and Comorbidity of Neuropsychiatric and Cardiometabolic Diseases

Sociotype and attachment might influence comorbidity of neuropsychiatric and cardiometabolic diseases acting on several biological pathways. Structures and mediators participating in attachment are also involved in the comorbidity of cardiometabolic and neuropsychiatric diseases [8, 9]. The concepts of allostasis and allostatic load have been championed by McEwen to describe how chronic stress “wear and tear” can affect well-being through over-action of adrenal steroid secretion and the activity of the sympathetic nervous system [10]. Nutrition (essential dietary-derived amino- and fatty acids for neurotransmitter synthesis, caloric restriction, and diet–gene interactions), is a major determinant of sociotype development during the human life cycle. Nutrition also influences growth and development, fertility and longevity, and also determines susceptibility to non-communicable diseases such as cardiovascular disease and cancer, and particularly diabetes and obesity, through in-utero effects, the diversity of gut microbiota and chronic stress [1].

6.1 Attachment and neuropsychiatric disorders

The origin of some mental pathologies is being sought in the attachment theory through the variations in the type of link that are established between primary caregivers of children since he/she is born until he or she becomes independent individual capable of taking care of him- or herself. Taking as a reference, the attachment theory, many studies have sought its influence on mental disorders such as the depressive or anxious disorders (internalized disorders) or behavior disorders (externalized disorders) and also in personality disorders such as the borderline personality disorder that has a prevalence of 1.6% to 5.9% in the general population [93]. There is a significant overlap between attachment, affective temperament, and personality that supports the value of attachment as a screen for personality disorders [2].

Nowadays, it is considered that the presence of insecure, anxious, avoidant or disorganized attachment results in a poor capacity to regulate emotions in the individual, leading to dysfunctional social and emotional development. Early anxious attachment or other forms of non-secure attachment are not psychopathologies by themselves nor are

they a direct cause of psychopathology. However, they constitute initiators of pathways probabilistically associated with later psychopathology [2].

There is a tight relationship between attachment and empathy, and children with secure attachment histories will be more responsive to the needs of others, showing increased empathy [2]. Empathy is defined as the capacity to perceive, share and understand others' affective states and, therefore, to imagine and feel what another person is experiencing without confusing the phenomenon with one's own direct experience [94]. The term empathy is also used to acknowledging another person's internal state, imagining the distress of others and what they are thinking or feeling when witnessing another person's suffering [95]. Empathy includes: experience sharing, mentalization by considering the other's states and their sources, and prosocial concern including being motivated to improve the other's experiences [18, 96]. Empathy emerges during the second year of life [17].

Deficits in socioemotional processing, especially the lack of empathy, are related to neurodevelopmental disorders as sociopathy [97] and other clinical conditions that involve social impairment and aggression such as conduct disorder [98] and disruptive behavior disorder [99]. Being able to understand other people's emotions and intentions is crucial for social interactions and well-being. Deficits in theory of mind functioning hamper this ability. In depression, there is a gender-specific impact of attachment styles on the theory of mind and possibly in other neuropsychiatric disorders.

Attachment provides the base for intimacy; the capacity for healthy protest and thus, detachment is the origin of autonomy. When non-attachment is prevalent, the capacity to reflect on one self and to dis-identify with painful or traumatic experience is impaired [100]. The four main abilities necessary for intimacy are the ability to seek care, the ability to give care, the ability to feel comfortable with an autonomous self, and the ability to negotiate. Therefore, a secure attachment is required to develop the capacity to participate in successful intimate relationships [101]. Deficiencies in the development of empathy and intimacy may underlie the appearance of anxious or depressive disorders in the adult.

Regarding the study of the possible mechanisms that underlie the link between attachment in early life and development of neuropsychiatric disorders in human adults, epigenetic changes have been evidenced in descendants from negligent mothers showing poor emotional regulation [102]. Furthermore, women that underwent psychological, physical or sexual violence during infancy have a higher risk of developing depressive disorders, anxious disorders or unstable personality than the general population [103]. They show impulsive behaviors, negative affection, identity problems and a poor affective regulation [104]. Babies born from these mothers also have an increased predisposition to undergo child abuse and negligence from their primary caregivers. Moreover, they reproduce the patterns of non-adaptive conducts such as psychoactive substance abuse, intense and unstable interpersonal relations, poor frustration tolerance and above all, a poor emotional regulation that characterized a number of neuropsychiatric disorders mainly anxious, depressive or personality disorders [105, 106]. There have

also been attempts to relate attachment to telomere length. However, the link seems to be indirect and mediated by mental stress [107] Stress is an important factor that shortens telomere length [9].

The therapist may profit from the type of attachment found in an individual. A precise responsiveness, attunement, and modulation of affect corresponds to secure or insecure attachment and can be utilized in the psychotherapist/patient relationship. The procurement of a secure base, the appearance of an autobiographical competence, the processing of affect, and the capacity to cope with loss are common to most effective psychotherapies and constitute a new interpersonal frame to the development of psychotherapy. The interrelationship between the environment and the brain is reflected in the way in which psychotherapy influences the biological mechanisms that occur in the brain. In the future psychotherapy might target specific functions in the brain [108, 109].

6.2. Attachment and cardiometabolic diseases

Attachment insecurity can be considered as a risk factor for the development chronic illness and might predispose to the comorbidity of cardiometabolic and neuropsychiatric diseases. Secure attachment has not been related to health conditions; however, anxious attachment is associated with poor health conditions, including stroke, heart attack, high blood pressure [3]. The environment in which early stages of life occur has effects on the developing of the orbitofrontal cortex. Development of this region is associated to attachment and determines some types of personality which are often associated to specific illnesses including the relation of Type A personality disorder with coronary heart disease [110]. There is an association between attachment-related anxiety and anxiety symptoms at follow-up in patients with cardiac diseases that are mediated by illness perceptions derived from different types of attachment. Attachment-related avoidance interacts with illness perceptions and lead to depressive symptoms at follow-up. Therefore, personality, cognitive appraisals, and emotional regulation play an important role in defining the coping abilities with illnesses [111].

Regarding metabolic diseases, an insecure attachment is related poor emotion regulation in children and might also be related to children's poor regulation of energy intake rendering children at risk for obesity [112]. Children with a poor regulation experience greater mental stress, which is linked to obesity [113, 114]. Problems with regulation of fear, sadness, and anger predict increased eating even in the absence of hunger [115-117]. Assessing the common types of attachment (secure, avoidant, anxious), and evaluating the affect regulation, interpersonal style, coherence of mind, and reflective functioning that accompany each type of attachment can guide interventions in the psychotherapy also for eating disorders [117].

7. Conclusion

The genotype and phenotype are associated to the risk (or resilience) to develop complex diseases. However, sociotype, which determines the way in which interactions between social, cultural and environmental influence health process is also determinant in the risk (or resilience) to develop diseases. Sociotype includes social and

cultural environmental factors, and attachment, which is the innate biological system that promotes a search for proximity between an infant and a bonding figure, forms part of it. Correct (or assertive) attachment increases the possibility not only for promote survival to a reproductive age but also determines empathy and intimacy that may underlie depressive and anxious disorders and cardio-metabolic disorders in the adult. The different types of attachment have physiological and endocrinological consequences that are the result of the exposure to stressful and/or traumatic events during early stages of life. Changes produced in the brain are long- term modifications that may be the result of epigenetic marks underlying risk to develop (or not) diseases in the adult. Therefore, sociotype and attachment might influence comorbidity of neuropsychiatric and cardiometabolic diseases mainly by epigenetically determining the development of brain structures and the expression of several neuroactive substance pathways that are involved in the comorbidity of cardiometabolic and neuropsychiatric diseases.

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Conflicts of Interest

The authors declare no conflict of interest.

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