Review article

Effects of maternal depression on the neurobiological and psychological development of children

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INTRODUCTION

Several studies have demonstrated that mothers and/or primary caregivers greatly influence the neurobiological and psychological development of children. Mothers seem to buffer stressors of the baby's internal and external world.[1,2] Such a protective behavior, associated to tactile, visual and auditory stimuli, as well as the translation and fulfillment of the babies' necessities, foster the development of genetically pre-programmed positive abilities.

The child's brain state of readiness to receive specific information from the environment has been referred to as "expecting the experience." It takes place especially during the first years of life, when the infant's brain development is considered to be pivotal and sensitive. These periods are crucial for the acquisition of social, affective and cognitive information, because it defines how many synapses are formed.[3,4] If the mother does not provide adequate protection and stimuli to the infant, the chances of damaging his or her neurobiological and psychological development processes increase significantly, which may lead to mean and long-term consequences.[5]

Perry & Polard consider that persistent failures in the manipulation of babies in their first months of life, especially the lack of a responsive look or conversation, contribute to decrease the number of neuronal connections or to their inadequate development. It has already been evidenced that mother's neglect of initial care, and physical and/or psychological abuse are associated to changes in the attachment pattern[6-8] and in the babies' motor and mental development.[9-12] Some authors have noticed a possible correlation among the first experiences of deprivation and the occurrence of depression, anxiety and drug abuse both in adults and children,[13] and borderline personality in adults.[14]

Moreover, some physiological and biochemical markers of stress have shown to be changed in children that underwent some kind of intense and persistent physical and/or psychological deprivation. Examples include: increased heart rate as compared to the control group,[15,16] changes in the circadian rhythm and levels,[12] changes in the urinary[10] and salivary[15,17] cortisol levels and

increased electroencephalogram (EEG) activity in the frontal right region as compared to the left region.[18,19]

Several studies carried out with non-human mammals stress the importance of the maternal care pattern in the initial phases of children development.[20-24] Variations in the genes expression of rodents and non-human primates undergoing stressful situations or that had suffered maternal deprivation in their early development phase have been observed. Some changes in different brain structures, neuro-hormonal secretions and density of specific receptors have also been evidenced. These changes have affected the way how these animals respond to stressors in the adult age.[20-24]

In humans, maternal neglect can occur even against the mother's will, as for example, due to postnatal depression (PND). The PND may account both for abuse and neglect,[7-10,25] especially when depressive symptoms are chronic.[8,10] Depressed puerperal women usually have an intrusive or withdrawn behavior pattern (emotionally absent),[25] which is harmful to children. PND is a depressive illness that typically occurs within the 4 and 12 postnatal weeks (CID10). It has a prevalence of 10 to 15% in the first two postnatal months; in 70% of mothers it can persist up to 6 months after the baby's birth.[9]

A number of neurological and behavioral findings in infants are associated to mother's depression, such as attachment pathologies,[8,26-28] EEG alterations,[18,19,29] and mental and motor development.[10] Infants of depressed women have more behavioral alterations, such as gaze aversion and reduced vocalization.[7,17,30,31]

It has been found that maternal depression during the infant's first year of life increased the frequency of significant EEG alterations,[32] cognitive alterations with learning deficit, depressant disorders and internalization symptoms.[33] It has been reported that maternal depression is associated to the increase in cortisol levels both in babies[17,34] and preschool-[35] and school-aged children.[36,37]

The goal of this study is to review the influence of maternal PND in children's development. Medline was searched for works from 1988 to 2004 with the following descriptors: maternal deprivation, maternal depression, PND, stress, brain plasticity, neglect, physical abuse,

psychological abuse, bad-treatment, salivary cortisol, limbic-hypothalamic-pituitary-adrenal (LHPA) axis, hypothalamic-pituitary adrenal (HPA) axis, cortisol, corticosterone, corticotrophin-releasing hormone (CRH), adrenocorticotropic hormone, babies, children and non-human mammals offsprings. Psychoanalytical literature about the development of the mother-infant relation was reviewed as well.

ENVIRONMENTAL INFLUENCE IN INFANTS' DEVELOPMENT

Pre-clinical studies

Research works strongly suggest that the arousal of a stress response pattern is resulting, at least partially, from the parental care pattern. This means that a nongenomic mode of inheritance can cause changes both in cell physiology and animal's behavior that can last their entire life time. The origin of personal differences is not clear yet, but two lines of studies with rodents have a favorable view towards considering the environment as a critical variant.[24]

In rats, neonatal stimulation consists of a tester handling the pups during some minutes in the two first weeks of life. The first line of evidence shows that pups manipulation accounts for a series of behavioral and neuroendocrine alterations in the adult offspring, like reduced fearfulness in response to novelty and an attenuate glucocorticoid production response, respectively. It is worth mentioning that this manipulation pattern stimulates mothers to be more careful: they lick and nurse their pups more frequently as compared to controls. Handling increases pup vocalizations, which have, in turn, been associated with increased maternal licking.[38] Lucion et al.,[39] Gomes et al.,[40] Severino et al.[41] and others were the first to demonstrate that neonatal stress alters reproductive mechanisms in the adult life. Lucion et al.[39] demonstrated that neonatal handling reduces the number of cells in the *locus coeruleus* of rats in about 35%.

The second line of evidence refers to the effect of maternal behavior in the development of endocrine and behavioral responses to the stressor. Extremely zealous mothers in the neonatal

period have adult pups that present the same behavioral and neuroendocrine response pattern as those submitted to early handling.

The BALB/c mice, a breed of mice that is usually very fearful and that has a high rate of HPA axis response to stress, were significantly less fearful and showed to have a low HPA axis response to stressors when raised by a C57 dam. C57 mothers are reported to lick and groom their pups twice as frequently as BALB/c mothers.[42]

These outcomes evidence an association between the manipulation pattern and maternal care in the neonatal period and between the behavior pattern and neural systems that mediate the responses to stressors in the offsprings as adults. These systems were shown to have an extraordinary plasticity, depending on the initial pattern of relationship with the environment.

Clinical studies

Some studies revealed that children grown up in orphanages, deprived from adequate stimuli, presented alterations during different levels of their development.

Spitz[43] observed two groups of babies raised in two different institutions. The first was an orphanage where the caregiver's team was constantly changing, so children were assisted by several different people, and could not count on the predictability and affection of a known and constant caregiver. The second institution was a nursery for babies of delinquent mothers. Mothers received orientation on how to provide basic care to their children; they were supervised and given advice. In both cases, babies had their basic needs regarding food and hygiene fulfilled. At the end of the study, the orphanage babies presented a significant delay in both intellectual and emotional development as compared to those from the nursery.

Carlson & Earls[12] assessed children in Romania who institutionalized and were extremely neglected during most of their life time.

The most frequent sequels of deprivation were mutism, unexpressive face, social shyness and bizarre stereotyped behavior.

Children aged between 2 and 9 months were separated in two groups: one control and one receiving physical and psychological stimuli throughout 1 year and 3 months. Findings evidenced that, when stimulated, children had an increased physical growth, and accelerated mental and motor development (Bayley scale) as compared to controls. Nevertheless, 5-6 months after the study had finished, none of these indexes was higher than those found in the control. Institutionalized children did not show to have a daily rhythm of cortisol secretion as compared to other Romanian children, the same age, raised by her parents at home. Their cortisol levels in the morning were significantly lower than those of parent-raised children, remaining high during the rest of the day, although it was not significantly high.

It is worth highlighting that in both groups there was an inverse significant correlation between the cortisol levels and mental and motor development (Bayley scale).

Gunnar & Donzella[44] studied Romanian children after 6.5 years of their adoption by English families. All of them had lived in orphanages up to 8 months prior to adoption, the majority being over 3 years of age when they started living with a family. Saliva samples were collected in the morning, in the afternoon and at night for 3 days. Their mean circadian rhythm of cortisol release was compliant to the expectations, however, when compared to Romanian children adopted soon after birth and to Canadian children raised with their original families, they had significantly higher levels of cortisol.

THE IMPORTANCE OF THE MOTHER-BABY RELATIONSHIP

Some psychoanalytic theoreticians pioneered in drawing attention to the importance of mothers in infants' development. They also tried to understand the psychodynamics of the mother-baby relationship.

Among them, Winnicott[45] introduced the idea of "primary maternal preoccupation," which is the mother's attitude of empathy with the child that allows her to understand and fulfill the baby's needs. He coined the term "good-enough mother," which refers to the mother who is able to tune

into the child's needs, and highlighted how important this empathy is for the baby's adequate mental development. The concept of primary maternal preoccupation is within the concept of holding environment, which relates not only to the function of physical support but also to psychological support.

Bion[46] introduced the concept of reverie, which is meant to be the mother's ability to think the baby's thoughts, name and assign meaning to them, while he or she is not able to do so, at least not adequately.

Bowlby[47] made a link between psychoanalytical theories and biology. He spanned these two fields of knowledge, and the findings of this union enriched our understanding of the mother-baby relationship. The neuropsychological structure that shapes the tie between babies and caregivers was named *attachment system.* This emotional and behavioral system was conceived as something innate and instinctual, very similar to hunger and thirst. It is a system that organizes the baby's memorization processes, which makes him/her strive for communication and proximity with the mother. Two experimental psychologists, Trevarthen & Aitken, expanded the scope of this system. They proposed that certain groups of neurons are genetically programmed and compose an "intrinsic motive formation" (IMF), which would originate the baby's brain capacity of developing an affective interaction. These authors consider that the baby's attachment is intersubjective and interpersonal. When the adult approaches the baby with adequate responsiveness, a fine rhythmic organization of synchronic or alternating responses can be triggered between them.[9]

The attachment system, from the evolutionist point of view, increases the baby's chances of survival, once an immature brain uses a mature one to fulfill its basic needs. An adequate link between the mother and the baby is crucial for the development of a safe attachment system, but the link must be fed by the baby's responsive behavior.

A safe attachment between the baby and the mother or other caregiver fosters the babies' well-being and their basic confidence on adults, while an unsafe attachment is related to increased

anxiety.[1,21,24,47,48] The parental response widens and strengthens the baby's positive emotional state and reduces the negative one,[6] signaling the need for parental action.

FINDINGS ABOUT HOW PND AFFECTS BABIES AND CHILDREN

EEG Alterations

Field et al.[19] investigated the asymmetry in the EEG of 3 to 6 month-old babies of depressed mothers with BDI>12, and compared it to the control group with BDI<9. The goal of their study was to determine whether depressed mothers and their babies presented an asymmetric right frontal EEG activation or not. The left frontal EEG activation has been associated with the expression of emotions related to closeness while the right frontal EEG activation has been associated with emotions that reflect affective withdrawal.[49] Twelve of 17 babies of depressed mothers had right frontal hyperactivity as compared to only 2 out of 15 babies of non-depressed mothers. The study did not reveal whether the asymmetry was due to the right or left lobe, but the authors stress that the identification of this asymmetry in babies aged less than 1 can be understood as a biological sign of vulnerability to the development of anxiety. The authors also considered that there may be an analogy between the babies' EEG pattern and the mother's typical depressed behavior, once babies are with their mothers during the examination. This should require an investigation on possible variants in the case mothers were not present.

In a study by Jonas et al.,[29] babies of depressed mothers were shown to have greater right than left frontal EEG activation when assessed in their first week of life, first month and at 3 months. Dawson et al.[18] examined the brain electrical activity of 13 to 15 month-old infants whose mothers suffered with depression. Infants of depressed mothers exhibited reduced left frontal activity during the baseline condition and during situations that are considered to deflagrate positive emotions as compared to controls. The same pattern was found in infants up to 3 years-old in another study.[32]

There are studies showing that inhibited babies are more likely to develop a right frontal asymmetry than controls. This would be both because of increased right frontal activity and left

frontal hypoactivity. Adults with depressive symptoms also exhibit right frontal asymmetry when compared to control groups; this alteration results from the hypoactivity of the left frontal region.[49]

Alterations in the vegetative nervous system (VNS) and HPA axis.

Alterations in babies

Field et al.[17] observed the interactions of 74 babies aged 3 to 6 months with their depressed (n=40) and non-depressed (n=34) mothers and with non-depressed adults. The interaction was tested through the "face-to-face"[25] paradigm combined with vagal tone assessment. Salivary cortisol was collected and both were used as stress markers. Babies of depressed mothers were shown to have a less positive interaction with strangers than controls, and their vagal tone did not increase as expected in this phase of development. These babies had a significantly higher heart rate (155.5 bpm) as compared to nondepressed mothers' babies (145.6 bpm) and significantly higher cortisol levels (2.6 ng/ml *versus* 1.1 ng/ml.) The vagal tone is necessary to inhibit the action of sympathetic nerves activity in the heart, and it reflects the maturation of the brain stem structures, controlling the heart rate pattern and its relation with breathing. The results of the study suggest a possible immaturity of the sympathetic nervous system of depressed mothers' babies. A limitation of this study is that authors did not assess baseline cortisol levels, which they only did after the interaction between the mother and the baby had taken place. Thus, it is not known if cortisol levels were high because of the acute stress resulting from the interaction with the mother or if they were high because of chronic stress. In both cases, the elevated levels can be resulting from the mothers' failure to protect the baby and buffer stressors, or due to higher genetic susceptibility of their HPA axis.

A preliminary study by Motta et al.[34] observed the association between maternal depression and HPA axis alterations in 6 month-old babies by assessing the salivary cortisol dosage by radioimmunoassay. Cortisol was collected from 8 babies of depressed mothers and 10 babies of nondepressed mothers at baseline and after 10 and 20 minutes after they were submitted to the

stressor “unexpressed face” (assessed by the MINI, EPDS and BDI tests). Preliminary data revealed a baseline cortisol level significantly higher in babies from mothers with depression ($p=0.003$) and a significant correlation between maternal BDI and baseline cortisol in babies ($r=0.58$; $p=0.011$). Even though these are very preliminary findings, they corroborate the hypothesis that the HPA axis of babies from depressed mothers had their functioning increased.

Bugental et al.[2] evaluated the effect of two variables, mother’s emotional withdrawal and corporal punishment, in the baseline cortisol and post-stressor levels of 44 babies under two years-old. Mother’s withdrawal was divided into: intentional, when mothers developed a strategic use of withdrawal as a control tactic during 2 years, and unintentional, when they suffered with maternal depression. Infants who experienced frequent intentional emotional withdrawal by their mothers showed elevated baseline levels of cortisol ($r=0.37$; $p<0.01$), but these numbers were higher when withdrawal was not intentional ($r=0.57$; $p<0.001$). The effect size (ES) estimate of withdrawal resulting from maternal depression was 0.94.

Several authors have suggested that the elevated production of glucocorticoids in the initial phases of infant’s development are in short-term associated to a way of dealing with stress that is not buffered by a suitable caregiver.[2,14,41,42]

Alterations in pre-school children

Essex et al.[35] analyzed 4.5 year-old children who had been exposed to stressors in the familial environment during their first year of life and who were or were not exposed to a stressor at the moment. Children were compared to two other groups: who had not been early exposed (first year) to stressors, and who were exposed or not to a familial stressor at the age of 4.5. A persistent exposure to stressors in the first year of life made the LHPA axis more sensitive when children were exposed to stressors at the age of 4.5. They presented significantly higher cortisol levels than those who had not been exposed to stressors in their first year of life and were or not exposed to stressors at the age of 4.5; and also than those who had been exposed in the past but were not at the age of

4.5. The most powerful predictor of elevated cortisol levels was the mother's PND in the infant's first year of life. The study suggests that children who had been exposed to stressors in the first year of life are more likely to undergo stressful situations later on their lives.

Alterations in school-aged children

A study performed by Lupien et al.[36] with 217 children from 6 to 10 years-old showed that children with low socioeconomic status present significantly higher levels of stress than children with high socioeconomic status, and this effect emerges as early as the age of 6. They also reported that children' cortisol level was significantly correlated with their mothers' extent of depressive symptomatology, regardless of sex ($r=0.22$; $p=0.004$). Familial income was negatively correlated to maternal depression scores ($r=-0.25$; $p=0.001$) and to levels of cortisol in children ($r=-0.31$; $p=0.001$). This suggests that the familial income is a significant predictor of both scores.

In a retrospective study, Ashman et al.[37] investigated how maternal depression was associated to internalizing symptoms and to salivary cortisol levels in children from 7 to 8 years-old. Forty-five 7 to 8 year-old children of mothers with a history of depression, and 29 children of nondepressed mothers were investigated. Children with internalizing symptoms (depressive emotion, anxiety, withdrawal and somatic complaints) whose mothers had a history of depression presented significantly elevated laboratory baseline cortisol levels. Presence of maternal depression in the first two years of life was a major predictor of elevated baseline cortisol level in children from 7 to 8 years-old. This was an evidence that exposure to maternal depression in the first two years of life can be associated to high cortisol levels later in life.

Alterations in behavior, and in the motor and mental development

Different studies have suggested that changes in behavior associated to maternal depression can happen in the earliest stages of development and affect the rest of the individual's life.

Alterations in babies (from 0 to 3 years-old)

Field et al.[17] videotaped 3 to 6 month-old babies in face-to-face interactions with their mothers and strangers for evaluation of their behavioral performance using a scale for interaction measurement. The infants of depressed mothers received lower ratings not only when interacting with their mothers, but generalized to their interactions with nondepressed adults as well. Besides presenting increased heart rate, babies of depressed mothers presented less vocalization ($p<0.001$) and avoided gaze more frequently ($p<0.001$) during interaction, both with their mothers and strangers, as compared to the control group. In most cases, the infants' behavior was not different between groups, but children of depressed mothers had higher gaze aversion (distant look) and decreased gaze toward the mother ($p<0.001$), which suggests that environmental factors may affect results.

Cohn & Tronick[25] assessed the interaction between depressive mothers and their 6 to 7 month-old infants. Maternal behavior was classified into three types: withdrawn, intrusive or adequate. Face-to-face interaction was examined for 3 minutes followed by a 40-minute spontaneous interaction. Withdrawn mothers did not play too much with their babies, rarely used motherese and presented sadness and poorly modulated affective behavior. Intrusive mothers demonstrated increased irritation with their babies and interfered in the infant's own and spontaneous actions. Adequate mothers were able to develop positive interactions with their babies. The behavioral descriptors used during the face-to-face interaction were coded and analyzed second by second. The authors found remarkable differences associated to withdrawn maternal and intrusive affective expression. Babies of withdrawn mothers were anguished, fussier, had difficulties engaging in social interaction and cried more, this means they complained more too. Infants of intrusive mothers increased gaze aversion (distant look) and decreased interaction with their mothers. Both groups of babies had a significantly less positive interaction ($p<0.001$) than babies of adequate depressive mothers. Positive mothers had a wider spectrum of behavior and affection.

In a sample of depressed mothers, 70% had chronic depression during their infant's first 6 months of life. At the age of 12, these infants showed delays in development (determined by the Bayley scale), mild neurological signals, reduced exploratory behavior and lower weight percentile.

Pickens & Field[30] found decreased positive expressions in 3 month-old babies of depressed mothers, which suggests an early depressive behavior. Mothers and their infants were videotaped in a 3-minute face-to-face interaction. The infant's facial expressions were identified with the AFFEX system (Izard & Dougherty, 1980) in which 10 facial expressions are coded (interest, joy, anger, sadness, surprise, fear, anguish, disgust, self-comfort, gaze aversion/distant look). Babies of depressed mothers presented significantly higher scores of negative expressions, they also remained more time with sad ($p<0.01$) and anger expressions ($p<0.01$) and showed lack of interest ($p<0.05$) for their mothers. They showed a preference for images with sad faces, which may be associated with the most usual expressions of their mothers.

Campbell et al.[26] assessed 67 dyads of depressed mothers and their infants and 63 dyads of mothers with sub-clinical symptoms or under remission and their infants. Mothers were all middle-class and married. They were videotaped while interacting with their babies at home when they were 2, 4 and 6 months-old. No significant differences were found between the groups in the face-to-face interaction, breastfeeding and playing at the age of 2 months. However, when the mother's depression extended up to six months after the baby was born (chronic depression), her expressions were compliant with anger and irritation, and the baby cried, screamed and became agitated, especially in face-to-face interactions. Mothers with chronic depression had less eye, physical and verbal contact during interaction and plays, they were less positive and emotionally engaged than those who had had a transient depression. These findings strongly suggest how important the distinction between transient and chronic (protracted) depression is when the effects on the baby's development are being considered.

The results of a study by Peláez-Nogueira et al.[50] suggest that by providing touch stimulation for their babies, the depressed mothers can increase infant positive affect and attention, and thus

compensate for negative effects resulting from their typical lack of affectivity during interactions. Their results should not be generalized, however, for authors used a homogeneous sample of adolescent mothers, and long-term effects of this kind of intervention were not studied yet.

Hipwell et al.[8] investigated 82 mother-infant dyads who were followed up over the children's first year of life. Twenty-five mothers met the criteria for unipolar depression: 9 had been admitted to a psychiatric unit, and 16 were outpatients. Even though a few residual symptoms remained at the end of the infant's first year of life, interaction disturbance was evident. The diagnosis of psychotic (with hospital admission) and non-psychotic depression (without hospital admission) was significantly associated to insecure attachment, which was assessed with the strange situation (SS) paradigm of Ainsworth.

Frankel & Harmon[27] investigated mother-child interactions and attachment pattern (SS) in a sample of 30 depressed and 32 nondepressed women (BDI) and their 3 year-old children. Depressed mothers were divided in three groups: episodic depression (n=13), dysthymia or chronic depression (n=7) and double depression (n=10). The way how depressed mothers described themselves and their babies was consistently more negative. Women with double depression were significantly less emotionally available and showed reduced affection and negative behavior ($p<0.03$) during SS. Infants of mothers with double depression presented more insecure attachment than the other two subgroups. The authors concluded that the consequences of maternal depression vary depending on type of depression, severity, and chronicity.

Martins & Gaffan,[28] in a meta-analysis including 7 studies, investigated the association between maternal depression and the attachment category using the SS paradigm. Babies of depressed mothers showed significantly reduced secure attachment and raised avoidant and disorganized attachment than the controls. The fact that the studies analyzed did not classified mothers as intrusive, withdrawn or adequate was considered a limitation. Two studies in which 12 month-old children were assessed did not make a correlation between insecure attachment and maternal depression, which impairs the assessment of the attachment category using SS. The

authors were very critical as to the selection of papers, carefully defining the characteristics of depressed and nondepressed mothers. The target-group mothers should present depressive symptoms that persisted all over the baby's life, and controls should not have been diagnosed with depressive disorder at any moment during the study. All infants had their attachment category assessed using the SS. Families should be predominantly free of problems such as parent's separation, bad-treatment or any other psychiatric symptom associated to the mother.

A large longitudinal study followed 1,215 dyads[51] from birth through 36 months; six visits were reported. At each visit mothers were assessed and categorized (CES-D; Radloff, 1997) as having chronic depression, depression at intervals and no depression. Children of mothers with chronic depression performed more poorly on measures of expressive language when interacting with their mothers (TE=0.43). They were considered less cooperative (TE=0.46) and as having more internalizing symptoms (depression, anxiety, withdrawal, somatic complains) and externalizing symptoms (aggressive and destructive behavior) (TE=0.62) when compared to children of mothers with depression at intervals and with no depression. Mothers with depression at intervals considered their children less cooperative (T=0.34) and with more internalizing and externalizing symptoms (TE=0.52) than children of mothers with no depressive symptoms. Maternal sensitivity was assessed as to supportive presence, respect for autonomy and absence of hostile behavior. They found that depressed mothers of lower social classes were less sensitive as compared to higher social class mothers, especially in cases of chronic depression. Besides maternal depression, maternal sensitivity was a strong predictor of school readiness, expressive language ($p<0.001$), and reduced problematic behavior ($p<0.05$).

Alterations in school children

Ashman et al.[37] found an association between internalizing symptoms and alterations in the HPA axis in children from 7 through 8 years-old of depressed mothers when submitted to stressors.

Malcarne et al.[33] compared distress correlates in a sample with 40 children from 8 through 12 years-old of depressed mothers and 46 of nondepressed mothers. They analyzed the association of depression, internalizing, externalizing and verbal ability problems with the maternal depression level, and the experience of traumatic events. Children of depressed mothers had significantly higher scores of depressive symptoms and internalizing and externalizing problems ($p<0.01$). Results indicated that depressive symptoms tended to be most consistently related to maternal depression. Child depressive symptoms were correlated with life events only for non depressed mothers. At-risk children with higher levels of verbal ability were significantly less likely to report depressive symptoms and internalizing and externalizing problems. The intellectual capacity may be a protection against stressors, even though these are only preliminary results. Moreover, the study does not examine the effect of maternal depression on the child's early development. We may assume, however, that mothers who were depressed during data collection are more likely to have developed depression at their baby's early development. This suggests that the child's problems may be related not only to the period of the study, but to an earlier stage.

DISCUSSION

The way how Winnicott,[45] Bion,[46] and Bowlby[47] developed their theories of the mind, including the concepts of good enough mother, maternal reverie and attachment system, respectively, was by intuitive observation and not following the scientific formal methodology. However, we start from theories like theirs to test scientific hypothesis. Moreover, the concepts that make possible to test them scientifically are too rudimentary to allow us to totally confirm or refute them. Experimental works that follow a formal scientific methodology have demonstrated a close relation between the pattern of primary care and the child's development. Research has confirmed such an association and has demonstrated alterations in neuroendocrine and behavioral systems of children who underwent privations and important stressful events in terms of intensity and lasting time in their early development.

The present review has demonstrated that depressed mothers usually do not have a good enough pattern of care, especially when depression lasts several months. The degree of severity and lasting period of depression and the mother's pattern of behavior (intrusive, withdrawn, and adequate) are likely to affect the quality of the mother-baby interaction. The attachment pattern accounts for alterations in EEG, HPA axis or in the Central Nervous System (CNS) and in the behavioral pattern of infants.

Although genetic mechanisms may play an important role in this association, it is evident that the mother-child interaction and motherhood quality should be considered important contributors to the individual's neurological, neuroendocrine and psychological development.

The studies outcomes demonstrate that depressed mothers have difficulties buffering stressors and promoting stimuli that favor the child's learning of appropriate and flexible ways of handling stressful situations.

The HPA axis is physiologically less responsive to stress after 2 to 3 months of age.[47] This contributes to the adequate development of infants, once they receive too many stimuli for their physical incapacity and lack of knowledge about the world that surrounds them. Several studies showed an association between early contact with maternal depression and alterations in the levels of cortisol. A higher sensitivity of the HPA axis to stressors is considered to occur in those babies. However, we found only two studies associating PND and abnormal levels of cortisol in babies of depressed mothers under the age of 1. They reported elevated levels in the first months of life, showing an increased activity of the HPA axis that would not be expected otherwise. Field's[32] study is not clear whether the elevated salivary cortisol levels are only caused by that specific moment of interaction or not, and the other study with altered baseline cortisol level presents only preliminary results.

We consider there is a lack of longitudinal studies about the baby's HPA axis behavior and maternal depression, which would compare short-, medium-, and long-term alterations and also check which the consequences and/or impairments resulting from elevated cortisol levels would be.

It is known that, at short term, the enhancement of glucocorticoids during stressors has an adaptive function,[52,53] however, chronic exposure contributes to the development of physical and mental pathologies.[35,54] As to cells, chronic stress can cause structural alterations with cells death and interruption of hypocampal neurogenesis, as well as alterations in the cellular immune system.[53,55] From the cognitive point-of-view, it can cause alterations in memory and learning. Moreover, the emotional response pattern to stressor may be altered as well.[12,13,35,54]

When both HPA axis and pattern of behavior were assessed, alterations occurred in both levels, thus the pattern of connection of mothers and babies, and the pattern of attachment and the development of the stress system (LHPA) are closely associated.

CONCLUSION

The genetic influence of maternal depression should not be ignored, as the child's mind become more susceptible. Research developed with animals strongly suggests that the arousal of a pattern of stress response occurs as a result, at least partially, of the parent's care pattern. This means that a nongenomic mode of inheritance can cause changes both in the cell physiology and in the animal's behavior during all its life time.

Studies involving manipulation and pattern of maternal care in non-human mammals have demonstrated that the environment affects the development of the behavioral and neuroendocrine system during the pups' life. Similarly, studies with human babies have evidenced that abuse and neglect affect the individual's development.[5,54]

Sometimes, the mother's style of emotional interaction can be more critical than the diagnosis of maternal depression, although there is a significant association between maternal depression and alterations in the mother-baby interaction.

Maternal depression seemed to have a smaller impact on the baby-mother relation and infant's development when other risk factors were not associated, as low husband's or family's support and low social economic status.

The importance of the initial stage of life for the individual's development should not be disregarded, once there are already many neuroendocrine, autonomic and psychological symptoms found in children that are associated to maternal depression. Familial, therapeutic and social support help women exert their motherhood properly.

Studies associating neurological, endocrine and behavioral alterations would help develop preventive measures to decrease morbidity of depressed mothers' children, like those that investigate how early LHPA axis alterations take place and which the medium- and long-term consequences of elevated cortisol levels are.

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ABSTRACT

Many recent studies have shown that maternal deprivation has important effects on the psychological and neurobiological development of the child. Puerperal depression, when persistent, predisposes to child abuse and negligence. This paper aims at reviewing studies published as of 1988 that demonstrated changes in the neurological, endocrine, mental and behavioral development of children born from depressed puerperal women. Environmental influence was also

revised, focusing on pre-clinical studies carried out with non-human mammals, which showed that deprivation or stress in early development stages predicts changes in brain structure, neuro-humoral secretions and density of specific receptors. Finally, the study also revises some theoretical aspects of the child-mother relationship importance, which are in accordance with the experimental findings.

Keywords: *Puerperal depression, maternal depression, infant, child, HPA axis, maternal deprivation, cortisol.*

Title: *Effects of maternal depression on the neurobiological and psychological development of children*

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