The Infant – Mother Connection and Implications for their Future Health

Part 1 – Positive maternal-child interaction during pregnancy

American College of Pediatricians - June 2018

ABSTRACT*:* The mother and unborn child impact each other's physiology and brain restructuring to help assure adaptation and bonding. The unborn child causes changes in the mother's nutritional status, in her immune system, and in the functioning of her brain that help assure optimal health for mother and child both before and after delivery. Conversely, the mother impacts her growing baby, in particular the baby's brain development, through her emotional state, sleep cycles, voice, and nutritional state. ACPeds encourages all health care professionals to promote policies that respect and protect the mother-baby duo with their intricately interconnected systems.

INTRODUCTION

A mother and her unborn child have unique interdependencies that are essential for the optimal health of each. After birth, these interactions continue as mother and child each benefit from the other's contribution to the relationship. This monogram explores some of the research that details this life-giving connection.

At the very onset of conception, dramatic changes begin – in mother, and, of course, in her child. New research describes the interaction between mother and child during pregnancy and early infancy, with an emphasis on the changes taking place in the central nervous system of each that promote maternal-infant attachment.

It is common knowledge that the unborn child grows and develops in utero, but less well known are the intricate ways in which the developing child influences many aspects of the mother's life, including her brain development. Likewise the mother impacts her child, even causing changes in the baby's sleep cycles and emotional responses.

OVERVIEW

This paper will first demonstrate the ways the mother is impacted by her pregnancy and the growing baby. The baby causes changes in the mother's nutritional status, in her immune system, and in specific areas of her brain which all serve to assure optimal health for mother and child.

Then the paper will discuss some of the ways the mother impacts her growing baby – through her emotional state, sleep cycles, voice and nutritional state. All these can influence the way the infant's brain is developing in utero.

Finally the paper will mention some of the ways after birth in which the growing child and mother influence each other and react in concert together.

A note on terminology: There are two medical terms for what we refer to in English as the *unborn baby* or *unborn child*: "*embryo"* refers to the baby during the first 8 weeks of his or her life (up to 10 weeks after the mother's last menstrual period), and "fetus" (Latin for "young one") refers to the baby during the remainder of his or her time in-utero

(from when all the organs have formed until birth). Because most of the research referenced in this paper does not differentiate between embryos and fetuses, we have chosen to use the all-inclusive term of unborn child in most instances.

I. DURING PREGNANCY – Mother impacted by pregnancy / infant

The mother's entire body is obviously affected by her pregnancy, but there are several ways in which the unborn baby directly impacts the mother that may not be as easily recognized. The baby , via hormonal influence, affects the mother's nutrition, alters her immune system, and directs the restructuring of the maternal brain.

Pregnancy presents the mother's body with unique challenges. Her body must be able to adequately nourish the new baby while assuring her own nutrition. In addition, the mother's immune system, which would normally identify the unborn as 'nonself' due to the baby's unique genetic code, must be down-regulated to allow the baby to develop without being rejected, while still maintaining a sufficient maternal defense against infection. Finally, the mother must adapt her motivational system to incorporate the care of a child who has numerous needs, yet is not able to demonstrate gratitude for the selfless acts of the mother.

Maternal nutrition

Nutritionally, a successful pregnancy is dependent upon the appropriate allocation of resources between mother and child. It is now known that the placenta is responsible for determining how these resources are allocated. No longer is the placenta viewed as a simple conduit of nutrition, but rather the placenta actively mediates metabolic signals from both mother and baby to assure optimal growth while maintaining maternal health.[1]

The influence of the unborn child on maternal nutrition begins when the young embryo influences the development of uterine blood vessels. The cytotrophoblast cells (that lie on the outer periphery of the developing embryo) secrete factors that stimulate vascular growth in the maternal uterus, including vascular endothelial growth factor and placental growth factor. Blood vessels are stimulated to remodel and form a more complex branching system of larger vessels, while, in addition, new blood vessels are formed. The placenta is forming and the uterus is preparing to support the new life.[2]

In addition, the placenta itself determines how nutrients are distributed between mother and child. Although the exact mechanisms are unknown, "the placenta senses and responds to changes in the maternal environment by altering its structure and function, which can lead to changes in blood flow, fetal nutrient supply, and secretion of hormones and other signaling molecules." [3]

Maternal growth factors, such as maternal insulin-like growth factor, leptin, and insulin all appear to affect the placental functioning, as do inflammatory mediators such as interleukin-6, and tumor necrosis factor alpha. In addition, the placenta may possibly determine how much nutrition the mother receives, based upon her own nutritional state. Research performed on mice at the University of Cambridge demonstrated the role the placenta may play. Mice were genetically altered so, when pregnant, placental growth and structure were impaired. The researchers then were able to manipulate the fetal and maternal environments to assess the role of the placenta. The authors state, "This study shows that the placenta fine-tunes the supply of maternal resources to the fetus via p110α in accordance with both the fetal drive for growth and the maternal ability to supply the required nutrients." [4]

Maternal Immune System

The placenta also influences the maternal immune system, with the interaction between the unborn child and maternal immune systems being complex and beyond the scope of this paper. But it is important to note that many cellular changes happen to assure the baby is not identified as 'foreign' and thus 'rejected' by the mother; to ensure the survival of a new and independent addition to the mother's life. The trophoblast cells that derive from the early embryo develop into the placenta that protects the unborn from the maternal immune system. These trophoblast cells specifically do not express

the paternal HLA antigens that would otherwise cause the mother to recognize the baby as foreign. Placental mRNA and microRNA may play a role in regulating the mother's immune system. In addition, the placenta produces hormones such as progesterone, and immune modulators such as prostaglandin E2, and interleukins 10 and 4 that impact the maternal immune system. As soon as the mother's body can respond to the developing embryo, her immune system changes so that immune modulating cells (leukocyte subpopulations) in her uterus alter their proportions. In addition, the endometrial natural killer population decreases, allowing the baby to survive. Other changes in the mother's immune system occur which "…allows for successful coexistence between the mother and the semi-allograft that is the fetus/placenta expressing both maternal (self) and paternal (nonself) genes." [5]

Maternal brain development

Pregnancy is a crucial period of time for central nervous system development as dramatic changes happen in the hormonal environment, helping prepare the maternal brain for motherhood. The "mommy" brain, about which many mothers laughingly complain, truly does exist – and further, it is caused by specific neuronal and hormonal alterations that occur during pregnancy and after delivery. These changes are all adaptive to enhance the ability of the mother to care for her infant.

Early in pregnancy, the levels of estrogen and progesterone greatly increase, and later oxytocin, prolactin, arginine vasopressin, and endorphins are released, causing a remodeling of the brain as some regions increase in number and size of neurons and cellular receptors, while other areas decrease. Neurotransmitters, including dopamine, norepinephrine, and serotonin are also instrumental in brain remodeling.

Affected areas include the regions controlling maternal behaviors such as nesting and protecting the young (medial preoptic area of hypothalamus), as well as the motivational system of the brain (amygdala / limbic system) and areas involved with memory and learning (hippocampus).

Overall brain size of the mother is reduced during pregnancy, with the changes beginning at the time of embryonic implantation. The hippocampus is one of the areas most affected. Using three-dimensional T1-weighted magnetic resonance volume images in 9 healthy pregnant women scanned before and after delivery, researchers documented a "reduction in brain size that was maximal at term and that reversed by 6 months after delivery," while the pituitary increases in size during pregnancy.[6]

Many of the changes in the maternal brain will assist the development of "maternal behavior" – a term characterized by the "caring and loving actions typically associated with caring and raising the young". [7] The medial preoptic area (mPOA) of the hypothalamus is the area most responsible for maternal behaviors. In this area hormones interface with cellular receptors to stimulate maternal behaviors.[8] Other areas involved include neural pathways that regulate emotions – neurons connecting the thalamus to the cingulate cortex.[9]

There is also an increase in estrogen-receptors alpha, especially in the medial preoptic area.[2] These receptors may make the mother more sensitive to estrogen which then stimulates maternal behaviors. Estrogen, in concert with cortisol, is likely also responsible for the recall memory deficits experienced by mothers during pregnancy and after delivery. 254 women participated in a study assessing verbal recall memory at three points in time (14 – 16 weeks gestation, 36 weeks gestation and 12 – 14 weeks postpartum). Women who had previously been pregnant scored worse at all times of gestation than those women who were pregnant for the first time. The effects on memory lasted for at least 3 months post-partum and those women who had experienced more pregnancies were more significantly affected.[10]

New brain cells are produced during pregnancy, most importantly in the hippocampus and in the subventricular zone of the lateral ventricles (SVZ). The new cells, mainly neurons, astrocytes, and oligodendrocytes, become fully integrated into preexisting circuits and allow the areas to respond to new stimuli. The hippocampus is significantly associated with learning and memory and the changes occurring in the hippocampus appear contradictory. The hippocampus acquires

new cells, so new learning can occur. But unnecessary neuronal pathways are eliminated, or pruned, making the region more efficient and leading to an overall decrease in hippocampal size.[2]

As early as 1940, researchers showed that the hormones estrogen and progesterone influenced maternal sexuality and behavior. Later, in 1980, endorphins, produced by the pituitary gland and hypothalamus, were noted to increase late in pregnancy.[9] Cortisol may also be involved in maternal behavior. In one study, first-time new mothers with higher cortisol levels were studied as they responded to their own baby's odor versus that of another infant. Those mothers with higher cortisol levels in their saliva responded more to their baby's odor than those mothers with lower levels.[8]

Towards the end of pregnancy, women have a dampened cortisol response to stress, which leads to lower changes in blood pressure, heart rate, and lower catecholamine responses. The 'down-regulation' of stress may be protective for both mother and child as delivery approaches.[10]

Maternal brains even change in ways that allow them to more effectively and efficiently respond to their infants. Researchers at Leiden University in Netherlands performed brain scans on women before pregnancy. Twenty-five women were rescanned after pregnancy and delivery. Brains showed a decrease in grey matter in regions associated with social cognition. These changes probably reflect pruning, making the brain function more efficiently and effectively in social attachment. Researchers could accurately differentiate scans performed on women who had given birth from those who had not become pregnant by tracking brain changes, and the observed changes persisted at follow up two years later.[11]

II. DURING PREGNANCY – Infant impacted by mother

Mothers influence their unborn children via maternal language, nutrition, and even sleep cycles.

Maternal voice and language

Infant bonding and attachment to the mother begins in utero and the two major senses involved in this bonding are hearing and smelling. A study showed that the baby recognizes and is excited by hearing the mother's voice in utero. Sixty babies were assigned to hear either tape recordings of the mother or a stranger reading a passage from a book. Fetal heart rate increased in response to the mother's voice, but decreased when exposed to the stranger's voice.[12] In another study, 40 babies at 36 weeks gestation who heard their mother reading aloud demonstrated learning of maternal voice.[13]

Infants born between 25 and 32 weeks gestation were exposed either to routine hospital noise or to the recordings of maternal sounds (voice and heartbeat). Those infants exposed to maternal sounds showed significantly larger auditory cortices bilaterally by cranial ultrasound one month after birth as compared to the control infants.[14]

The baby recognizes the native language of its mother in utero and prefers it to other languages. At two days of age, 16 infants were evaluated while listening to either English or Spanish audiotapes and demonstrated preference for their mothers' native language.[15]

The baby can even remember words heard while in utero. Unborn babies exposed to new 'pseudowords' in utero demonstrated memory of those words when exposed to them after delivery as evaluated by EEG.[16]

Maternal diet and odors

The unborn baby is bathed in the amniotic fluid, and swallows many ounces of this liquid each day, experiencing various odors and tastes based on maternal diet and environment. The baby is thus being programmed to prefer these same odors and tastes later on to enhance bonding with the mother.

Amniotic fluid has been shown to be affected by maternal diet. In one study, mothers ingested garlic or placebo prior to amniocentesis, and the odor of garlic was identified in the amniotic fluid in 4 of the 5 women who had ingested garlic.[17] By 13 – 15 weeks gestation the taste buds of the fetus have developed and are in contact with the amniotic fluid, so the baby is potentially impacted by tastes imparted by the maternal diet. In fact, they have been shown to remember tastes they have experienced in utero. Researchers divided 56 pregnant women into three groups – those who drank carrot juice during pregnancy only, those who only drank carrot juice after the baby was born and those who never drank carrot juice. Infants at five months of age were presented with two kinds of baby cereal – with and without carrot flavoring. The babies who had been exposed to carrot juice in utero were more accepting of the carrot flavored cereal.[18]

Maternal sleep cycles

"A clear day-night rhythm of fetal heart rate synchronized with maternal rest-activity, heart rate, cortisol, melatonin and body temperature rhythms is found in humans" which develops in the last trimester.[19] A diurnal rhythm in the basal heart rate was found in 73% of babies in utero who were monitored on continuous 24 hour recordings between 26 and 38 weeks gestational age, and this was closely related to the maternal heart rate rhythm.[20]

III. DURING PREGNANCY – Infant and mother impact each other

The mother and her unborn child impact each other in other ways, including their heart rates and even their movements. Using a technique involving "Transfer Entropy" that measures the interaction between two variables, researchers showed maternal heart rate influences the fetal heart rate by 26-31 weeks of gestation, and that influence increases with increasing gestation for most pregnancies. The unborn child, in turn, influences maternal heart rate but this effect decreases with gestation. [21] Movements in utero also appear to raise maternal heart rate and skin conductivity. [22] In return, mother's movements and laughter cause the baby to move.[23]

IV. IMMEDIATELY AFTER BIRTH - Infant brain development impacted by mother

Just as the infant's brain was affected by the mother during pregnancy, interactions with the mother continue to impact the child's brain development for many years. Here we will highlight the changes occurring immediately after birth.

Newborn Senses

The newborn is immediately attracted to the smell of amniotic fluid, but quickly transitions to prefer the breast scent of the mother. In one study 22 newborns up to 3.5 days old, who had been breastfed 6-24 times, were observed as they lay on a warming bed. Babies preferentially moved at least 13 cm to get to breast pads that had their own mother's scent on them, but not for clean pads.[24] Newborns have demonstrated they can be soothed simply by exposure to maternal odors, while breastfed infants have been noted to respond differently to maternal odors than do formula fed infants.[25,26]

The newborn also shows early preferences for hearing the mother's voice. Babies have shown they recognize their mother's voice at 2 – 4 days after birth. In one study infants were able to cause a recording of their mother's voices or another woman's voice to play depending on how vigorously they sucked on a pacifier. These infants preferentially caused maternal recordings to be played.[27, 28]

Newborns recognize songs parents sang to them while in utero, and they prefer to hear a book that was read to them in utero. Newborns also prefer to hear strangers who are speaking their mothers' native language rather than a new / foreign language.[15]

The newborn infant's ability to distinguish between mother and other is dependent upon amygdala functioning. In animal research, monkeys whose amygdala had been damaged were less able to signal their distress or pick out their mother from other monkeys.[29]

V. AFTER BIRTH - Maternal Brain Development impacted by infant

The mother's brain continues to change after her infant is born, especially in those areas that impact maternal behavior towards her infant. Brain regions utilized in senses such as smelling, hearing, and vision are affected to enhance maternal bonding.

Although not often acknowledged or recognized, the olfactory system is involved in maternal-infant bonding. The olfactory system develops connections to the media preoptic area region of the hypothalamus as well as to the limbic/reward system, so the mother quickly recognizes the smell of her own infant.[26]

The mother's visual centers are enhanced so she prefers viewing her own infant. Functional MRIs performed on right-handed mothers who watched videos of their own infants versus watching unknown infants demonstrated enhanced blood oxygenation in several regions of the brain – bilateral precuneus, right superior temporal gyrus and left amygdala.[30] Interestingly, these changes were associated with the mothers' reports of their perceived warmth towards their infant. The amygdala also demonstrates an increase in activity in the weeks after giving birth. This reward center of brain 'lights up' when mother looks at her baby. MRI scans show the amygdala responded more when mothers looked at photos of their own babies versus photos of other infants).[31]

Just as the infant's amygdala is shaped by maternal interactions, so the mother's amygdala is altered after delivery. The amygdala, in conjunction with the nucleus accumbens and the medial prefrontal cortex form a network that is important in social functioning. The neurotransmitter, dopamine, is active in these regions of the mother's brain after birth, and helps promote maternal-infant bonding. Mothers who demonstrated more synchronous behavior with their infants during observation in the home setting were found to have increased dopamine responses on functional MRI-PET scans while viewing videos of their infants versus unfamiliar infants.[32]

A greater amygdala response was linked to lower maternal anxiety and fewer symptoms of depression. The amygdala has higher concentration of receptors for oxytocin which makes mothers more responsive to her baby's needs and the oxytocin receptors mean the mother receives pleasure, motivating her to continue mothering behaviors. Oxytocin increases after delivery when women look at their babies or hear their babies coo or cry, as well as increasing during breastfeeding. Most likely due to the elevation of oxytocin with breastfeeding, breastfeeding mothers showed a greater level of brain (including in the amygdala) responses to their babies' cries compared with formula feeding mothers in the first month postpartum in one small study.[33] It may be that the elevated levels of oxytocin also help negate negative maternal experiences by dampening the cortisol and neural responses.[34]

The relationship between healthy amygdala functioning in the mother and maternal-infant bonding is further demonstrated in a study of 42 first time mothers. Seventeen of the mothers were identified as having unresolved trauma or loss in their lives. All mothers underwent functional MRI scans while viewing photos of their own infants' happy or sad faces as well as unknown infants' happy or sad faces. Those mothers who had unresolved trauma were noted to have a blunting of their amygdala response to the sad faces of their own infants, possibly impacting their caretaking and responsiveness.[35]

CONCLUSION

This paper serves to highlight some of the many ways the mother and unborn child impact each other's physiology and brain restructuring. The amazingly intricate interconnected systems demonstrate the uniqueness of each pregnancy and encourage all health care professionals to promote health care policies that respect and protect the duo.

Primary Authors: Jane Anderson, MD, FCP and Patricia Lee June, MD, FCP
June 2018

The American College of Pediatricians is a national association of licensed physicians and healthcare professionals who specialize in the care of infants, children, and adolescents. The mission of the College is to enable all children to reach their optimal physical and emotional health and well-being.

REFERENCES

1. Diaz P, Powell TL, and Jansson T. The Role of Placental Nutrient Sensing in Maternal-Fetal Resource Allocation. *Biology of Reproduction*. 2014; 91(4):82, 1-10.

2. Hillerer KM, Jacobs VR, Fischer T, and Aigner L. The Maternal Brain: An Organ with Peripartal Plasticity. *Neural Plasticity.* 2014; http://dx.doi.org/10.1155/2014/574159

3. Dimasuay KG, Boeuf P, Powell TL and Jansson T. Placental Responses to Changes in the Maternal Environment Determine Fetal Growth. *Frontiers in Physiology*. 2016; 7(12):1 -9.

4. Amanda N. Sferruzzi-Perri, Jorge López-Tello, Abigail L. Fowden, and Miguel Constancia. Maternal and fetal genomes interplay through phosphoinositol 3-kinase(PI3K)-p110α signalling to modify placental resource allocation. *PNAS*, September 2016 DOI: 10.1073/pnas.1602012113

5. Abrahams VM, et al Immunology of the maternal-fetal interface. *UpToDate*. December 16, 2015.

6. Oatridge A, Holdcroft A, Saeed N, et al., "Change in brain size during and after pregnancy: study in healthy women and women with preeclampsia," *American Journal of Neuroradiology*, vol. 23, no. 1, pp. 19–26, 2002.

7. Nugent, P. (2018). What is MATERNAL BEHAVIOR? definition of MATERNAL BEHAVIOR (Psychology Dictionary). [online] Psychology Dictionary. Available at: http://psychologydictionary.org/maternal-behavior/

8. Bridges RS. Neuroendocrine Regulation of Maternal Behavior. *Frontiers in Neuroendocrinology*. 2015; 0:178-196

9. Kinsley CH and Lambert KG. The Maternal Brain. *Scientific American*. January 2006; 72 – 79

10. Glynn LM. Increasing Parity Is Associated with Cumulative Effects on Memory. *Journal of Women's Health*. 2012; 21(10): 1038-1045.

11. Hoekzema E, Barba-Muller E, et al Pregnancy leads to long-lasting changes in human brain structure. *Nature Neuroscience* 2017; 20:287-296

12. (Kisilevsky BS, Hains SMJ, et al Effects of Experience on Fetal Voice Recognition. *Psychological Science*. May 2003 vol 14 3:220-224

13. Voegtline KM, Costigan KA, et al. Near-term fetal response to maternal spoken voice. *Infant Behavior and Development*. 2013 36(4):

14. Webb AR, Heller HT, Benson CB, Lahav A. Mother's voice and hearbeat sounds elicit auditory plasticity in the human brain before full gestation. *PNAS.* 2015; 112 (10)3152-3157.

15. Moon C, Cooper RP, Fifer WP Two-day-olds prefer their native language. *Infant Behavior and Development.* 1993. 16(4):495–500.

16. Partanen E, Kujala T, et al. Learning-induced neural plasticity of speech processing before birth. *Proceedings of the National Academy of Sciences*. 2013; 110(37):15145-15150.

17. Mennella JA, Johnson A, and Beauchamp GK. Garlic ingestion by pregnant women alters the odor of amniotic fluid. *Chemical Senses*. 1995; 20(2):207-9.

18. Mennella jA, Jagnow CP, and Beauchamp GK. Prenatal and Postnatal Flavor Learning by Human Infants. *Pediatrics* 2001; 107(6):E88.

19. Mirmiran M, Maas YGH, Ariagno RL. Development of fetal and neonatal sleep and circadian rhythms. *Sleep Medicine Review.* 2003;7(4): 321-334.

20. Lunshof S, Boer K, Wolf H, van Hoffen G, Bayram N, Mimiran M. Fetal and maternal diurnal rhythms during the third trimester of normal pregnancy: outcomes of computerized analysis of continuous twenty-four-hour fetal heart rate recordings. *American Journal of Obstetrics & Gynecology*. 1998;178(2):247-54.

21. Marzbanrad F, Kimura Y, et al. Quantifying the Interactions between Maternal and Fetal Heart Rates by Transfer Entropy *PLOS One.* December 23, 2015 p 1-13.

22. Glynn LM and Sandman CA. Prenatal Origins of Neurological Development – A Critical Period for Fetus and Mother. *Current Directions in Psychological Science*. December 5, 2011http://journals.sagepub.com/doi/abs/10.1177/0963721411422056?journalCode=cdpa

23. Hopson, Janet L. Fetal Psychology. Psychology Today. September 1, 1988. https://www.psychologytoday.com/articles/199809/fetal-psychology

24. Varendi H and Porter RH. Breast odour as the only maternal stimulus elicits crawling towards the odour source. *Acta Paediatrica*. 90:372 – 5, 2001

25. Sullivan RM and Toubas P. Clinical Usefulness of Maternal Odor in Newborns: Soothing and Feeding Preparatory Responses. *Biology of the Neonate*. 1998; 74(6):402-408.

26. Vaglio S. Chemical communication and mother-infant recognition. *Communicative & Integrative Biology*. 2009; 2(3):279-281

27. DeCasper AJ, Fifer WP. Of human bonding: newborns prefer their mothers' voices. *Science.* 1980; 208(4448):1174-6

28. Hepper PG, Scott D and Shahidullah S Newborn and fetal response to maternal voice. *Journal of Reproductive and Infant Psychology*. 1993 (11):147-153

29. Bauman MD, Lavenex P, et al. The Development of Mother-Infant Interactions after Neonatal Amygdala Lesions in Rhesus Monkeys. *Journal of Neuroscience*. 2004; 24(3):711-721

30. Wan MW, Dwoney D, et al. The Neural Basis of Maternal Bonding. *PLOS ONE.* 2014 9(3):e88436

31. Leibenluft E, Gobbini M, Harrison T, Haxby J Mothers' neural activation in response to pictures of their children and other children. *Biological Psychiatry*. 2004; 56 (8):225-232"

32. Atzil S, Touroutoglou A, et al. Dopamine in the medial amygdala network mediates human bonding. *PNAS* (Proceedings of the National Academy of Sciences USA). 2016, 114(9):2361-2366.

33. Kim P, Feldman R, et al. Breastfeeding, brain activation to own infant cry, and maternal sensitivity. *Journal of Child Psychology and Psychiatry*. 2011; 52(8):907-15

34. Rupp HA, James TW, et al. Amygdala response to negative images in postpartum vs nulliparous women and intranasal oxytocin. *Social Cognitive and Affective Neuroscience*. 2014; 9(1): 48 – 54.

35. Kim S, Fonagy P, et al. Mothers' Unresolved Trauma Blunts Amygdala Response to Infant Distress. *Society for Neuroscience*. 2014; 9(4):352-363.