NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

# Infant Mental Health

## Neurobiology of Attachment

*Self-Study*

**Contributors:**
Saira Kalia, MD
Mireya Nadal-Vicens, MD, PhD

The theory of human attachment, introduced by John Bowlby around sixty years ago, has significantly influenced developmental psychology by providing a framework for understanding how individuals form and maintain social bonds (Bretherton, 1994). Bowlby's attachment theory has generated an extensive body of research and conceptual elaborations, making a notable impact on the field of developmental psychopathology (Ein‐Dor et al., 2010). This theory has also been applied to various domains, such as understanding the impact of attachment on the parent-child dyad in pediatric care (Kaiser et al., 2018), implications for counseling adolescents (Genuis, 1994), and even exploring humanity's shifting attachment to the natural world (Jenkins, 2023).

Research has shown that attachment experiences have a significant impact on an individual's emotional and behavioral processes. The release of oxytocin, a hormone associated with social bonding, has been noted to play a role in the formation of attachments (Johnson & Young, 2015). Additionally, studies have shown that early experiences of attachment can alter the way that the brain processes emotions and social cues in adulthood (Schore & Schore, 2007). Attachment security in infancy has been linked to prospective links to brain morphometry in late childhood, indicating the long-term impact of attachment experiences on brain development (Leblanc et al., 2017). Furthermore, attachment representation has been found to moderate the influence of emotional context on information processing, suggesting a neurophysiological impact of attachment history on emotional processing (Leyh et al., 2016). Moreover, the neural basis underlying the trait of attachment anxiety and avoidance has been revealed by the amplitude of low-frequency fluctuations and resting-state functional connectivity, shedding light on the neurobiological mechanisms underlying different attachment styles (Deng et al., 2021).

The parent-infant relationship plays a crucial role in setting the neurobiological tone for the infant brain, influencing stress handling and attachment development. Self-regulation, which is essential for both the caregiver and child, is vital for forming secure attachments. Stress can impede self-regulation and be transmitted from caregiver to child, thereby affecting attachment formation. Therefore, promoting self-regulation and minimizing stress transmission is essential for attachment development (Insel & Young, 2001; Perry et al., 2017; Landers & Sullivan, 2012; Mueller & Tronick, 2019; Orehek et al., 2017; Alexander et al., 2022; Heylen et al., 2016; Fumagalli et al., 2018).

The prenatal period is critical for the parent-infant relationship, with maternal factors impacting the developing fetus through various mechanisms such as the maternal Hypothalamic-Pituitary-Adrenal (HPA) axis, placental epigenetics, mitochondrial dysfunction, immune system activation, and the maternal microbiome (Sheng et al., 2021; Barrett & Swan, 2015; Sanchez-Aranguren & Nadeem, 2021; Abu-Raya et al., 2016; Leis et al., 2019; Fouda et al., 2018;Rosario et al., 2019; Xu et al., 2014; Hohwü et al., 2015; Dauby & Flamand, 2022; Jahan et al., 2023). Maternal stress and environmental factors during pregnancy have been associated with alterations in fetal growth, oxidative stress, and mitochondrial dysfunction, which can impact the development of the fetal brain and stress response systems (Sheng et al., 2021; Sanchez-Aranguren & Nadeem, 2021; Abu-Raya et al., 2016; Leis et al., 2019; Fouda et al., 2018; Riddell et al., 2007; Rosario et al., 2019; Xu et al., 2014; Long et al., 2023;; Dauby &

Flamand, 2022; Veazey et al., 2017; Jahan et al., 2023). These alterations can have long-term implications for the offspring's neurodevelopment and stress response, highlighting the significance of the prenatal environment in shaping the parent-infant relationship and the infant's future well-being.

A growing body of evidence suggests that trauma can be passed down across generations through genetic mechanisms. Women who experienced the Tutsi genocide while pregnant had children with alterations in their stress response systems and changes in their genomic makeup (Perroud et al., 2014). Additionally, there is evidence that trauma experienced by fathers can also be passed down to their children, likely through changes in the chromatin of their sperm (Yehuda et al., 2014). Animal studies have also provided support for these findings, showing that trauma experienced by male rodents can be passed down to their offspring through epigenetic changes in sperm. These findings indicate that there are biological processes in place that can transmit trauma across multiple generations (Dias and Ressler, 2014).

The connection between maternal stress and negative infant outcomes has been acknowledged for some time. We are learning that maternal stress can lead to changes in fetal brain development which can have an impact on the child's stress response system throughout their life. Studies have shown that stress experienced during pregnancy can lead to long-term alterations in the HPA axis of infants, which can be observed at various stages of development including 6 months, 5 years, and even 10 years after birth. (Lupien et al., 2009; Buss et al., 2010; O Donell et al., 2014).

Perinatal stress has been found to have a significant impact on the HPA axis and its ability to respond to stress in the child's environment. This can be attributed to the modification of the genetic material (chromatin) surrounding genes involved in the stress response, a process known as an epigenetic modification (Bhattaria, 2021). This can lead to the transmission of altered stress responses across generations. Additionally, prenatal maternal stress has been linked to changes in specific brain regions that play a crucial role in emotional regulation, such as the hippocampus's size and the amygdala's reactivity (Qiu et al., 2015; Rifkin-Graboi et al., 2015). The effects of significant prenatal stress may even extend to the child's cognitive functioning later on in life (Davis and Sandman, 2010). This can be explained by the exposure to stress hormones (glucocorticoids); studies have shown that in the absence of external stress, administration of glucocorticoids is associated with smaller hippocampal size in both infants and monkeys (Lupien et al., 2009).

It can be challenging to differentiate the various forms of distress that can occur during the perinatal period, such as health anxiety, medical issues, psychosocial stress, anxiety disorders, pregnancy-related anxiety, depressive disorders, and PTSD. However, specific maternal mental health conditions, such as anxiety and depressive disorders, have been linked to many of the same negative outcomes in infant neurodevelopment caused by chronic stress during pregnancy (Wu et al., 2022). These outcomes can include changes in the HPA stress axis, decreased size of the hippocampus, and increased reactivity of the amygdala. These findings suggest that these specific mental health conditions can have a profound impact on the developing fetus and should be given proper attention and support during the perinatal period. (Qiu et al., 2015; Rifkin-Graboi et al., 2013, 2015). These changes in stress response can manifest in a variety of ways, including changes in the HPA stress axis, decreased hippocampal size, and increased amygdala reactivity (Qiu et al., 2015; Rifkin-Graboi et al., 2013, 2015). These findings underscore the importance of identifying and treating mental health conditions in expectant mothers in order to promote optimal development for their children.

Interestingly, recent research has suggested that selective serotonin reuptake inhibitors (SSRIs) may have the ability to reverse the effects of prenatal stress exposure on the brain (Borue 2007). Studies using rodent models have shown that SSRIs can reverse the decrease in hippocampal volume that is typically seen in animals exposed to prenatal

stress (Rayen et al., 2011). This is an exciting area of research, as it suggests that interventions such as SSRI treatment may be able to mitigate some of the negative effects of prenatal stress exposure on the developing brain.

**Role of Oxytocin and Dopamine**

The parent-infant relationship is a complex interplay of nature and nurture that begins at birth and continues to evolve throughout the early years of life. The bond between a parent and an infant is thought to be mediated by two key neurobiological pathways: the dopaminergic "reward" pathway and the oxytocinergic system. The dopaminergic pathway is involved in the regulation of reward and motivation and is activated by positive social interactions, such as those that occur between a parent and an infant. Research has shown that the release of dopamine in response to a positive social interaction is positively correlated with the strength of the parent-infant bond (Strathearn et al., 2009)

In addition to the dopaminergic pathway, the oxytocinergic system also plays a crucial role in the parent-infant bond. Oxytocin is a hormone produced in the hypothalamus that is involved in a wide range of physiological processes, including labor and lactation. Oxytocin is linked to prosocial effects, such as improved social memory, improved eye gaze when looking at faces, improved recognition of faces and facial expressions, and increased trust manifestations (Baumgartner et al., 2008; Domes et al., 2007; Guastella et al., 2008a, 2008b; Kosfeld et al., 2005; Savaskan et al., 2008). This suggests that oxytocin plays a key role in the positive social interactions between parents and infants, and in the development of the parent-infant bond. Both mother-infant and father-infant pairs exhibit these effects (Kim et al., 2014; Scatliffe et al., 2019; Vittner et al., 2018). Additionally, oxytocin is thought to be important in the emergence and maintenance of the behaviors that form the foundation of the parent-infant bond. Studies have shown that oxytocin is released in response to stimuli such as infant suckling or the sight or sound of an infant, and is thought to mediate a wide range of behaviors related to the parent-infant bond, such as physical contact, synchrony, and responsiveness (McNeilly et al., 1983; Kim et al., 2014).

**Role of Physical Contact**

Physical contact plays a crucial role in infant neurodevelopment, influencing various aspects of attachment and cognitive development. Research has shown that physical contact, such as skin-to-skin care and holding, positively impacts neurodevelopmental outcomes in premature infants (Vanderveen et al., 2009). Additionally, studies have demonstrated that physical contact, including maternal nurturing behavior, such as licking and grooming, can lead to genetic changes and modifications in the stress response receptors, influencing long-term neurodevelopmental outcomes .

This concept was demonstrated in animal models by Meaney and Szyf (2005) as well. On the other hand, decreased licking and grooming in infancy resulted in higher stress levels in adult rodents (Meaney and Szyf, 2005; Weaver et al., 2004). Notably, we found that licking caused genetic changes in one of the stress response receptors that the animal had adopted for the rest of its life (Francis et al., 1999; Weaver et al., 2004). Similar epigenetic DNA changes have been discovered in humans. The discovery that the DNA structure in rodents that encodes stress response molecules is similar to the DNA structure in humans who have a history of child abuse and later commit suicide (McGowan et al., 2009) has important implications for understanding the long-term effects of early life stress on mental health. This may help to explain why individuals who have experienced child abuse are at a higher risk for mental health conditions such as depression and suicide.

It is important to note that this research is still in the early stages and more studies are needed to fully understand the mechanisms behind these findings. However, it does highlight the need for early intervention and support for individuals who have experienced childhood trauma to mitigate the negative effects on mental health in adulthood. Physical contact between a mother and her child has significant clinical benefits. One such form of physical contact is Skin-to-skin contact (SSC) which has been shown to have clear benefits for both mother and newborn after birth,

such as assisting the newborn's transition to extrauterine life, increasing breastfeeding rates, and promoting early parent-infant bonding (United Nations Children's Fund and World Health Organization 2009). Because of these advantages, SSC is now required as part of the World Health Organization's (WHO) Baby-Friendly Hospital Initiative (United Nations Children's Fund and World Health Organization 2009). SSC has been recommended as the standard of high-quality care for all newborn infants, regardless of gestational age, geographical location, or socioeconomic environment, due to its efficacy, cost-effectiveness, and feasibility. Studies have shown that SSC can lead to improved physiological stability, enhanced mother-infant bonding, and increased breastfeeding success, among other benefits.

The following infant benefits of skin-to-skin contact have been demonstrated:

- Improved Thermoregulation
- Decreased crying
- Increased breastfeeding initiation
- Heart rate variability regulation
- Decreased pain and distress
- Improved breathing patterns and oxygen saturation levels
- Improved sleep
- Improved digestion and weight gain
- Improved survival and shorter neonatal intensive care unit admission for premature infants

(Cleveland et al., 2017; Hendricks-Munoz et al., 2015; Mitchell et al., 2013; Moore et al., 2016; Rojas et al., 2003; Samra et al., 2013; Widström et al., 2019)

Given this information, it is clear that nurturing and skin-to-skin contact play a crucial role in the neurodevelopment of infants. The research discussed above highlights the importance of physical contact in promoting healthy stress regulation and emotional response in both animal and human models. The absence of physical contact, on the other hand, has been linked to long-term changes in stress tone and neurobiology, which can negatively impact cognitive and emotional development. (Feldman & Eidleman, 2003; Welch et al., 2015) Studies have shown that a lack of physical contact during infancy can lead to deficits in global brain function, attention, IQ, verbal and executive functioning, working memory, and learning. (Nelson et al., 2007) These changes can be attributed to the fact that physical contact plays a critical role in the development of the nervous system. Early physical contact helps to regulate the stress response and promotes the formation of neural connections that support cognitive, emotional, and social development. Therefore, parents and caregivers need to ensure that infants receive adequate nurturing and physical contact to promote optimal neurodevelopment. Additionally, healthcare providers should prioritize promoting the use of skin-to-skin contact as a standard of care for newborn infants in order to support the emotional and cognitive development of the child.

The role of physical contact in infant neurodevelopment is crucial, as research has shown that infants who lack physical contact, such as those who are institutionalized or raised in orphanages, have a higher risk of developing cognitive and behavioral problems. These children are more likely to have lower IQ scores and experience difficulties with attention, working memory, and learning (Aita et al., 2021). Furthermore, the absence of physical contact during infancy has been linked to long-term changes in stress tone and neurobiology, which can negatively

impact cognitive and emotional development (Flacking et al., 2012). Studies have also demonstrated that childhood neglect and lack of physical contact can lead to an increased risk of mental health problems such as depression and anxiety in adulthood (Yoshida & Funato, 2021). However, it is important to note that these changes are not irreversible, as nurturing and skin-to-skin contact can help mitigate the negative effects of lack of physical contact during infancy. Providing physical contact to infants who have been deprived of it can help improve their cognitive, emotional, and social development, highlighting the importance of providing infants with a nurturing environment that includes physical contact, such as skin-to-skin contact, to support their healthy development (Koo et al., 2014; Oguz et al., 2018; Velandia et al., 2010; Maastrup et al., 2017; Li et al., 2023; Little et al., 2018; Gribble et al., 2020; Marlette et al., 2022; He et al., 2021; Kobus et al., 2022; Levinsen et al., 2021; Tsai et al., 2021; Bigelow & Williams, 2020; Ball et al., 2006; Wehby & Trujillo, 2017; Svensson et al., 2020; Jiang et al., 2020; Skinner & Narchi, 2021; Potgieter & Adams, 2019; Chiu et al., 2005; He et al., 2020; Aita et al., 2020).

The clinical implications of this issue were recently highlighted during the COVID-19 pandemic. Initially, there were talks of separating mothers with suspected or proven COVID-19 infection from their newborns to reduce the risk of transmission (Stuebe, 2020). However, the World Health Organization recommended against separation, stating that infants with suspected or confirmed COVID-19 mothers should be "enabled to stay together, practicing skin-to-skin contact." This highlights the tension between the desire to reduce the risk of transmission and the known clinical benefits of physical contact. The Centers for Disease Control and Prevention also initially advised facilities to "consider separating the mother from her infant" until the mother was deemed no longer contagious. This further highlights the importance of balancing the risk of infection with the known benefits of physical contact, particularly during infancy when the brain is still developing.

The critical period of pregnancy and postpartum is crucial for the development of both the infant and the parents. It's a time of increased risk for mental illness but also a time for the developing fetus and infant to develop stress response, emotional regulation, and a sense of security in relationships. By addressing the parent-infant relationship, attachment and health, medical and mental health providers can have a positive impact on families and future generations. Physical contact and parental nurturing behaviors can lead to epigenetic changes that can override heritable traits. Mental health conditions may interfere with nurturing behaviors, but early detection and intervention can lead to better self-regulation in the infant and improve psychoemotional well-being as they grow and develop. Mental health clinicians can help by observing and understanding parent-infant interactions and exploring parent perceptions of the infant and themselves as parents, particularly in the setting of pregnancy and postpartum mood or anxiety disorders

**References**


1. Abu-Raya, B., Smolen, K. K., Willems, F., Kollmann, T. R., & Marchant, A. (2016). Transfer of maternal antimicrobial immunity to hiv-exposed uninfected newborns. Frontiers in Immunology, 7
2. Alexander, S. L., Frederico, M., & Long, M. (2022). Improving attachment security in early childhood intervention: a framework from constructivist grounded theory. Journal of Early Intervention, 45(4), 408-429
3. Aita, M., Faugère, G. D. C., Lavallée, A., Feeley, N., Stremler, R., Rioux, É., … & Proulx, M. (2021). Effectiveness of interventions on early neurodevelopment of preterm infants: a systematic review and meta-analysis. BMC Pediatrics, 21(1)

4. Barrett, E. S. and Swan, S. H. (2015). Stress and androgen activity during fetal development. Endocrinology, 156(10), 3435-3441.
5. Baumgartner T, Heinrichs M, Vonlanthen A, et al: Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. Neuron 58(4):639–650, 2008 18498743
6. Bretherton, l. (1994). The origins of attachment theory: john bowlby and mary ainsworth.. A Century of Developmental Psychology., 431-471
7. Bhattarai, S., & Ferreira, J. J. (2021). Epigenetic modifications and its basic mechanism. Journal of innovative agriculture, 8(1), 19-25
8. Borue, X., Chen, J., & Condron, B. G. (2007). Developmental effects of SSRIs: lessons learned from animal studies. *International journal of developmental neuroscience : the official journal of the International Society for Developmental Neuroscience*, *25*(6), 341–347
9. Buss, C., Davis, E. P., Muftuler, L. T., Head, K., Sandman, C. A., & High, P. C. (2010). Maternal cortisol over the course of pregnancy and subsequent child amygdala and hippocampus volumes and affective problems. Proceedings of the National Academy of Sciences, 107(22), 11655-11660
10. Cleveland L, Hill CM, Pulse WS, et al: Systematic review of skin-to-skin care for full-term, healthy newborns. J Obstet Gynecol Neonatal Nurs 46(6):857–869, 2017 28950108
11. Dauby, N. and Flamand, V. (2022). From maternal breath to infant's cells: impact of maternal respiratory infections on infants ‘immune responses. Frontiers in Pediatrics, 10.
12. Davis EP, Sandman CA. The timing of prenatal exposure to maternal cortisol and psychosocial stress is associated with human infant cognitive development. *Child Dev*. 2010;81(1):131-148
13. Deng, M., Zhang, X., Bi, X., & Gao, C. (2021). Neural basis underlying the trait of attachment anxiety and avoidance revealed by the amplitude of low-frequency fluctuations and resting-state functional connectivity. BMC Neuroscience, 22(1)
14. Dias, B., Ressler, K. Parental olfactory experience influences behavior and neural structure in subsequent generations. *Nat Neurosci* 17, 89–96 (2014)
15. Ein‐Dor, T., Mikulincer, M., Doron, G., & Shaver, P. R. (2010). The attachment paradox. Perspectives on Psychological Science, 5(2), 123-141
16. Francis D, Diorio J, Liu D, et al: Nongenomic transmission across generations of maternal behavior and stress responses in the rat. Science 286(5442):1155–1158, 1999 10550053
17. Feldman and Eidelman "Skin-to-skin contact (Kangaroo Care) accelerates autonomic and neurobehavioral maturation in preterm infants" Developmental medicine & child neurology (2003)
18. Flacking, R., Lehtonen, L., Thomson, G., Axelin, A., Ahlqvist, S., Morán, V. H., … & Dykes, F. (2012). Closeness and separation in neonatal intensive care. Acta Paediatrica, 101(10), 1032-1037
19. Fouda, G. G., Martinez, D. R., Swamy, G. K., & Permar, S. R. (2018). The impact of igg transplacental transfer on early life immunity. ImmunoHorizons, 2(1), 14-25
20. Fumagalli, M., Provenzi, L., Carli, P. D., Dessimone, F., Sirgiovanni, I., Giorda, R., … & Montirosso, R. (2018). From early stress to 12-month development in very preterm infants: preliminary findings on epigenetic mechanisms and brain growth. Plos One, 13(1), e0190602
21. Genuis, M. (1994). Long-term consequences of childhood attachment: implications for counselling adolescents. International Journal for the Advancement of Counselling, 17(4), 263-274
22. Guastella AJ, Mitchell PB, Dadds MR: Oxytocin increases gaze to the eye region of human faces. Biol Psychiatry 63(1):3–5, 2008a 17888410
23. Guastella AJ, Mitchell PB, Mathews F: Oxytocin enhances the encoding of positive social memories in humans. Biol Psychiatry 64(3):256–258, 2008b 18343353
24. Hendricks-Muñoz KD, Xu J, Parikh HI, et al: Skin-to-skin care and the development of the preterm infant oral microbiome. Am J Perinatol 32(13):1205–1216, 2015 26007311

25. Heylen, J., Vasey, M. W., Dujardin, A., Vandevivere, E., Braet, C., Raedt, R. D., … & Bosmans, G. (2016). Attachment and effortful control. The Journal of Early Adolescence, 37(3), 289-315
26. Hohwü, L., Graversen, L., Li, J., Sørensen, T. I. A., & Obel, C. (2015). Prenatal parental separation and body weight, including development of overweight and obesity later in childhood. Plos One, 10(3), e0119138
27. Insel, T. R. and Young, L. J. (2001). The neurobiology of attachment. Nature Reviews Neuroscience, 2(2), 129-136
28. Jahan, F., Vasam, G., Green, A. E., Bainbridge, S., & Menzies, K. J. (2023). Placental mitochondrial function and dysfunction in preeclampsia
29. Johnson, Z. V. and Young, L. J. (2015). Neurobiological mechanisms of social attachment and pair bonding. Current Opinion in Behavioral Sciences, 3, 38-44.
30. Jenkins, M. (2023). Mother nature: applicability to contemporary attachment styles. Australasian Psychiatry, 32(2), 135-137
31. Kaiser, S., Zimmet, M., Fraser, J., Liddle, K., & Roberts, G. (2018). Recognition of attachment difficulties and developmental trauma is the responsibility of all paediatricians. Journal of Paediatrics and Child Health, 54(10), 1110-1116
32. Kim M, Kang SK, Yee B, et al: Paternal involvement and early infant neurodevelopment: the mediation role of maternal parenting stress. BMC Pediatr 16(1):212, 2016 27955632
33. Koo, W., Tank, S., Martin, S. L., & Shi, R. (2014). Human milk and neurodevelopment in children with very low birth weight: a systematic review. Nutrition Journal, 13(1)
34. Kosfeld M, Heinrichs M, Zak PJ, et al: Oxytocin increases trust in humans. Nature 435(7042):673–676, 2005 15931222
35. Landers, M. and Sullivan, R. (2012). The development and neurobiology of infant attachment and fear. Developmental Neuroscience, 34(2-3), 101-114
36. Leblanc, É., Dégeilh, F., Daneault, V., Beauchamp, M. H., & Bernier, A. (2017). Attachment security in infancy: a preliminary study of prospective links to brain morphometry in late childhood. Frontiers in Psychology, 8
37. Leis, K., Mazur, E., Jabłońska, M., Kolan, M., & Gałązka, P. (2019). Endocrine systems of the skin. Advances in Dermatology and Allergology, 36(5), 519-523
38. Leyh, R., Heinisch, C., Kungl, M., & Spangler, G. (2016). Attachment representation moderates the influence of emotional context on information processing. Frontiers in Human Neuroscience, 10
39. Li, L., Ji, F., Wang, Y., Wang, L., Yu, L., Wu, X., … & Hu, X. (2023). The clinical experience of early skin-to-skin contact combined with non-nutritive comfort sucking in mothers of preterm infants: a qualitative study. BMC Pregnancy and Childbirth, 23(1)
40. Little, E. E., Legare, C. H., & Carver, L. J. (2018). Mother–infant physical contact predicts responsive feeding among u.s. breastfeeding mothers. Nutrients, 10(9), 1251
41. Marlette, B., Einspieler, C., Niehaus, D. J., Unger, M., & Jordaan, E. (2022). Maternal mental health and infant neurodevelopment at 6 months in a low‐income south african cohort. Infant Mental Health Journal, 43(6), 849-863
42. McGowan, P., Sasaki, A., D'Alessio, A. *et al.* Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. *Nat Neurosci* 12, 342–348 (2009)
43. McNeilly AS, Robinson IC, Houston MJ, et al: Release of oxytocin and prolactin in response to suckling. Br Med J (Clin Res Ed) 286(6361):257–259, 1983 6402061
44. Meaney MJ, Szyf M: Maternal care as a model for experience-dependent chromatin plasticity? Trends Neurosci 28(9):456–463, 2005 16054244
45. Mitchell AJ, Yates C, Williams K, et al: Effects of daily kangaroo care on cardiorespiratory parameters in preterm infants. J Neonatal Perinatal Med 6(3):243–249, 2013 24246597

46. Moore ER, Bergman N, Anderson GC, et al: Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database Syst Rev 11(11):CD003519, 2016 27885658
47. Mueller, I. and Tronick, E. (2019). Early life exposure to violence: developmental consequences on brain and behavior. Frontiers in Behavioral Neuroscience, 13
48. Nelson CA3rd, Zeanah CH, Fox NA, et al: Cognitive recovery in socially deprived young children: the Bucharest Early Intervention Project. Science 318(5858):1937–1940, 2007 18096809
49. O'Donnell, K. J., Glover, V., Barker, E. D., & O'Connor, T. G. (2014). The persisting effect of maternal mood in pregnancy on childhood psychopathology. Development and Psychopathology, 26(2), 393-403
50. Orehek, E., Vazeou-Nieuwenhuis, A., Quick, E., & Weaverling, G. (2017). Attachment and self-regulation. Personality and Social Psychology Bulletin, 43(3), 365-380
51. Perroud N, Rutembesa E, Paoloni-Giacobino A, et al. The Tutsi genocide and transgenerational transmission of maternal stress: epigenetics and biology of the HPA axis. *World J Biol Psychiatry*. 2014;15(4):334-345. doi:10.3109/15622975.2013.866693
52. Perry, R. E., Blair, C., & Sullivan, R. M. (2017). Neurobiology of infant attachment: attachment despite adversity and parental programming of emotionality. Current Opinion in Psychology, 17, 1-6
53. Rayen I, van den Hove DL, Prickaerts J, et al: Fluoxetine during development reverses the effects of prenatal stress on depressive-like behavior and hippocampal neurogenesis in adolescence. PLoS One 6(9):e24003, 2011 21912658
54. Riddell, R. P., Stevens, B., Cohen, L. L., Flora, D. B., & Greenberg, S. (2007). Predicting maternal and behavioral measures of infant pain: the relative contribution of maternal factors. Pain, 133(1), 138-149
55. Rifkin-Graboi, A., Kong, L., Sim, L. *et al.* Maternal sensitivity, infant limbic structure volume and functional connectivity: a preliminary study. *Transl Psychiatry* 5, e668 (2015)
56. Rojas MA, Kaplan M, Quevedo M, et al: Somatic growth of preterm infants during skin-to-skin care versus traditional holding: a randomized, controlled trial. J Dev Behav Pediatr 24(3):163–168, 2003 12806228
57. Rosario, F. J., Gupta, M. B., Myatt, L., Powell, T. L., Glenn, J. P., Cox, L. A., … & Jansson, T. (2019). Mechanistic target of rapamycin complex 1 promotes the expression of genes encoding electron transport chain proteins and stimulates oxidative phosphorylation in primary human trophoblast cells by regulating mitochondrial biogenesis. Scientific Reports, 9(1)
58. Samra NM, Taweel AE, Cadwell K: Effect of intermittent kangaroo mother care on weight gain of low birth weight neonates with delayed weight gain. J Perinat Educ 22(4):194–200, 2013
59. Sanchez-Aranguren, L. and Nadeem, S. (2021). Bioenergetics adaptations and redox homeostasis in pregnancy and related disorders. Molecular and Cellular Biochemistry, 476(11), 4003-4018
60. Schore, J. R. and Schore, A. N. (2007). Modern attachment theory: the central role of affect regulation in development and treatment. Clinical Social Work Journal, 36(1), 9-20
61. Sheng, J. A., Bales, N. J., Myers, S. A., Bautista, A. I., Roueinfar, M., Hale, T. M., … & Handa, R. J. (2021). The hypothalamic-pituitary-adrenal axis: development, programming actions of hormones, and maternal-fetal interactions. Frontiers in Behavioral Neuroscience, 14
62. Savaskan E, Ehrhardt R, Schulz A, et al: Post-learning intranasal oxytocin modulates human memory for facial identity. Psychoneuroendocrinology 33(3):368–374, 2008 18221838
63. Scatliffe N, Casavant S, Vittner D, et al: Oxytocin and early parent-infant interactions: a systematic review. Int J Nurs Sci 6(4):445–453, 2019 31728399
64. Stuebe A: Should infants be separated from mothers with COVID-19? First, do no harm. Breastfeed Med 15(5):351–352, 2020 32271625
65. Qiu A, Anh TT, Li Y, et al. Prenatal maternal depression alters amygdala functional connectivity in 6-month-old infants. *Transl Psychiatry*. 2015;5(2):e508. Published 2015 Feb 17

66. Vanderveen, J. A., Bassler, D., Robertson, C. M., & Kirpalani, H. (2009). Early interventions involving parents to improve neurodevelopmental outcomes of premature infants: a meta-analysis. Journal of Perinatology, 29(5), 343-351
67. Veazey, R. S., Lu, Y., Xu, H., Ziani, W., Doyle-Meyers, L. A., Ratterree, M. S., … & Wang, X. (2017). Maternal antibodies against tetanus toxoid do not inhibit potency of antibody responses to autologous antigen in newborn rhesus monkeys. Journal of Medical Primatology, 47(1), 35-39
68. Vittner D, McGrath J, Robinson J, et al: Increase in oxytocin from skin-to-skin contact enhances development of parent-infant relationship. Biol Res Nurs 20(1):54–62, 2018 29017336
69. Weaver ICG, Cervoni N, Champagne FA, et al: Epigenetic programming by maternal behavior. Nat Neurosci 7(8):847–854, 2004 15220929
70. Welch et al. "Family Nurture Intervention in the Neonatal Intensive Care Unit improves social‐relatedness, attention, and neurodevelopment of preterm infants at 18 months in a randomized controlled trial" Journal of child psychology and psychiatry (2015)
71. Widström AM, Brimdyr K, Svensson K, et al: Skin-to-skin contact the first hour after birth, underlying implications and clinical practice. Acta Paediatr 108(7):1192–1204, 2019 30762247
72. Wu, Y., Espinosa, K. M., Barnett, S. D., Kapse, A., Quistorff, J. L., Lopez, C., Andescavage, N., Pradhan, S., Lu, Y. C., Kapse, K., Henderson, D., Vezina, G., Wessel, D., du Plessis, A. J., & Limperopoulos, C. (2022). Association of Elevated Maternal Psychological Distress, Altered Fetal Brain, and Offspring Cognitive and Social-Emotional Outcomes at 18 Months. *JAMA network open*, *5*(4), e229244
73. Xu, L., Sun, Y., Gao, L., Cai, Y., & Shi, S. (2014). Prenatal restraint stress is associated with demethylation of corticotrophin releasing hormone (crh) promoter and enhances crh transcriptional responses to stress in adolescent rats. Neurochemical Research, 39(7), 1193-1198
74. Yehuda R, Daskalakis NP, Lehrner A, et al. Influences of maternal and paternal PTSD on epigenetic regulation of the glucocorticoid receptor gene in Holocaust survivor offspring. *Am J Psychiatry*. 2014;171(8):872-880
75. Yoshida, S. and Funato, H. (2021). Physical contact in parent-infant relationship and its effect on fostering a feeling of safety. iScience, 24(7), 102721