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Parental Instincts: The Neurological and Biological Factors Associated with Parenthood

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**Parental Instincts: The Neurological and Biological Factors
Associated with Parenthood**

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HONR 401: Honors Thesis

Advisor: Dr. Meredith Rowe

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Abstract

The following project involves a systematic review of the scientific literature on neural and biological changes of mothers and fathers in parenthood. Until very recently, little scientific research was devoted to studying how bearing children affects a man or woman's long-term biology. Over the last twenty years, studies of neuroplastic changes in new mothers show specific neural mechanisms responsible for altering the behaviors of mothers during and after pregnancy. These changes in neuroplasticity alter behavior in such a way that led to mothers requiring less sleep and being more prone to hearing the cries of their children. In addition to these neural changes, fetal cell migration through the placenta plays a role in the biology of mothers, including both disease onset and prevention. Scientists today seek to understand the correlation between motherhood and its effects on the lifespan of the woman. Recent studies suggest that mothers are not the only parent to undergo physical changes after becoming a parent. Even though men are not directly involved in the childbearing process past fertilization, fathers undergo changes in their neural and biological pathways as well. As humans have co-parented for the majority of human history, many fathers are subject to hormone fluctuations and increases in adipose tissue as a survival mechanism to aid in many sleepless nights ahead once their baby is born. Current research continues to answer more questions regarding how becoming a parent affects long-term health and longevity.

Acknowledgements

Regarding the completion of this Undergraduate Honors Thesis, I would like to thank Dr. Brett Niblack M.D. of Atrium Health for sparking my interest in the biology and neurology behind maternal and paternal behavior. By countless conversations in the clinic and hospital floors, his influence has greatly broadened by interests in science towards things I never imagined I would be passionate about. Secondly, I would like to thank Dr. Meredith Rowe for agreeing to be my thesis mentor and for pushing me to reach my greatest potential in science. Finally, I would like to thank Honors Director, Dr. Wilson Hawkins, for putting in the work necessary to get high performing students to national conferences, TSD dinners, and thesis presentations.

I. Introduction

From an evolutionary perspective, the goal of each species is to live long enough to reproduce. This constant effort to maintain the survival of the species is oftentimes fatal to many animal species throughout the wild. The human experience of parenthood, however, has displayed itself quite differently. Due to the nearly two decades of time it takes to raise a human being to full maturity, parenthood in humans is a much more involved process both emotionally and biologically. Spanning from fertilization until full maturation, the changes that men and women experience as parents are rooted in biology. While one might consider these changes to simply be “maternal instinct” or “natural parenting genes” displayed after becoming a parent, many characteristics of new mothers and fathers are deeply grounded in the fields of neuroscience, endocrinology, and molecular genetics (Tucker, 2022).

Throughout pregnancy and postpartum, the female brain is exposed to increasingly escalating levels of hormones, mainly due to the placenta. These hormone fluctuations affect the neuroplasticity of women within the hippocampus, a brain area well known for its role in regulating learning and memory. Hippocampal volume is often used as an indicator for brain health, and it has correlation with memory and dementia risk (Brecht et al., 2018). These brain changes within mothers show associations (Figure 1) with various affective disorders such as depression and/or anxiety. Hormonal changes also lead to behavioral changes through neuromodulator changes affecting a mother’s ability to distinguish infant cues that trigger caretaking behaviors. Even the age at which a woman undergoes childbirth may be correlated to longevity among older mothers compared to nonparous women. Other hormonal changes, such as the relationship between estrogen and progesterone also play roles in regulation of maternal behavior.

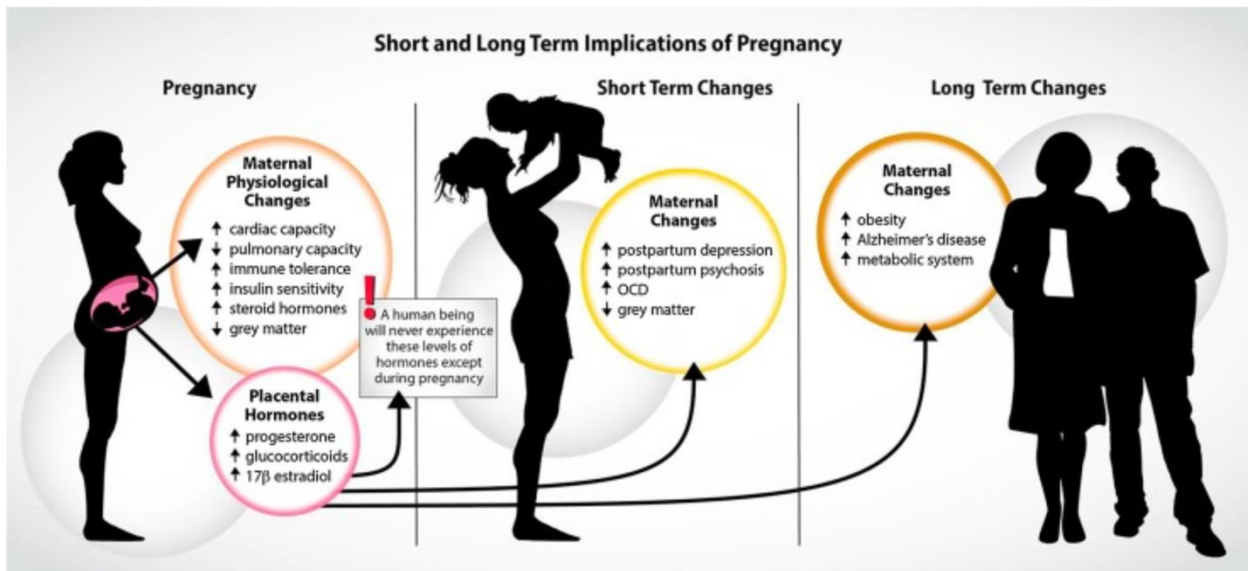


Figure 1. Short- and Long-Term Implications of Pregnancy due to Biological Changes (Duarte-Guterman et al., 2019)

Researchers have observed the phenomenon that an estrogen surge following a progesterone withdrawal at parturition has an important role in initiation of the biology behind maternal behavior in animal models with application to humans. The surge of estrogen upon parturition has an important job by modulating the anxiety levels of the mother and initiating the mother's approach to their pups or infant, respectively. The three main hormones present at birth, estrogen, progesterone, and cortisol steadily increase throughout gestation and drop around the time of labor. These hormones, and others discussed later, have been shown to regulate neuroplasticity, neuroinflammation, and behavior in new mothers. These alterations in maternal brain function drive specific behaviors necessary for infant survival and affect health outcomes for mothers as they age. Hormones and parturition also increases certain associations with obesity and certain neurodegenerative diseases, such as Alzheimer's disease.

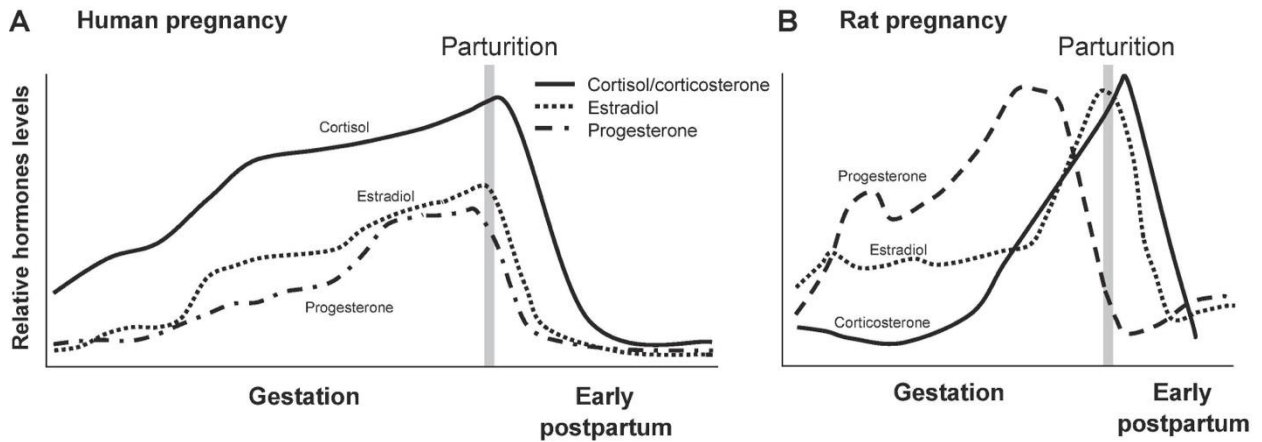


Figure 2. Hormone profiles during human (A) and rat (B) pregnancy and early postpartum. Based on data from (Brunton et al., 2010).

While not directly involved in the process of childbearing much after fertilization, the fact that humans have predominantly co-parented across history is responsible for a variety of changes within the biology of fathers. Many biological mechanisms have evolved to aid in the survival of fathers upon the arrival of the infant, including paternal weight gain and fat storage. This additional fat storage provides energy for the father who historically was tasked with hunting and providing the food necessary for the family to survive and thrive (Garfield et al., 2016). Endocrinological changes also take place within fathers that increases caretaking behaviors. Hormonal fluctuations of cortisol, testosterone, and prolactin drive many of these endocrine changes, and often lead to greater feelings of father-infant bonding soon after birth (Garfield et al., 2016). These mechanisms are important due to their potential ability to knit the family structure together through biological changes in both parents after the arrival of a child.

When studying the changes associated with parenthood, it is crucial to account for the difference in these changes associated with the sex of the parent. The neurobiology of the mother transitions towards introducing neural circuits necessary to caring for their infant,

including affinity to recognize infant cries and other cues needed to provide maternal care (Brecht et al., 2018). While males can become fathers up into their old age, pregnancy and childbirth becomes more dangerous for women with each passing year after 35-40 years old. With this increased risk towards older mothers, some researchers also believe that there is also greater reward due to potential associations between older ages at birth and longevity in women (Shadyab et al., 2017). Mothers naturally undergo hormonal changes due to carrying the fetus in pregnancy, while males typically undergo endocrinological changes in response to the changes within the mother.

II. Maternal Neurological Changes and Instinct

Over the past couple of millennia, childbirth and childrearing has become a more socialized activity than ever before in human history. Even as humans migrated from hunter-gather tribes towards modern civilizations, the social aspect of childbirth and childrearing has yet to alter the neuro-endocrine structures responsible for maternal behaviors. During labor and in the first couple of months after giving birth to their child, women find themselves performing various maternal tasks that often were never taught or observed prior to performing them (Odent, 2009). Within modern culture, many women never even observe a delivery of a baby until they are delivering their own. Because of this, women often face more anxiety and distress prior to delivery than one might have experienced historically. Despite this lack of exposure to delivery prior to their own, women often display the same instincts and neurological phenomena due to the evolution of the female brain over previous millennia of giving birth and mothering children. A prime example of this occurrence is the fetus ejection reflex within women during childbirth.

A true fetus ejection reflex is observed when a human baby is born after a short series of irresistible contractions that leave no room for any voluntary movements. During these circumstances, the neocortex of the mother has reduced its control of the archaic brain structures that oversee vital biological functions such as giving birth (Odent et al., 2009). In these times such as these, even civilized women can be found behaving in irrational ways that would normally be seen as socially unacceptable: they often shout, swear, are rude to others, and appear insane. Their entire personality often appears cut off from the outside world, unaware of external events. During a fetus ejection reflex, even the calmest of women

often find themselves in the most unique quadrupedal postures and experience a strong urge to grasp hold of something (Odent et al., 2009).

At the moment of birth until a few minutes after, mothers appear as if they are in a sort of orgasmic or exhilarated state. This usually occurs right after the first eye-to-eye contact between mother and baby. When asked to report about the experience in retrospect, new mothers describe the experience as a joyful emotional state that their body flows into soon after birth (Odent et al., 2001). After delivery of the baby and placenta, women experience a sudden drop in their estrogen and progesterone levels which causes the hormone prolactin to take over. Prolactin is the hormone that is responsible for milk production. After birth, neonates soon begin exhibiting a rooting reflex, which starts when the corner of the baby's mouth is stroked or touched. Depending on the direction of the stroking, the baby will turn his or her head and open his or her mouth to follow this direction of the stroking as a mechanism to find the breast or bottle to begin feeding. This surge in prolactin begins the process for a complementary behavior that is well-adapted within mammals: spontaneous initiation of lactation within the first hour after delivery.

Within the last few decades of studying neuroplasticity, scientists have largely come to an agreement that while children's brains are malleable and plastic, most changes neuroplasticity halt around the age of 25. After reaching this milestone of the mid-twenties, an adult's brain becomes mature and fully wired. This "wiring" within neuroplasticity is defined as "a final common pathway of neurobiological processes, including structural, functional, or molecular mechanisms, that result in stability or compensation for age or disease related changes" (Smith, 113). What is odd about neuroplasticity is that these statements are starting to be refuted, with newer research showing motherhood being

associated with dramatic changes in both short-term and long-term brain function. These changes range from pregnancy and early postpartum periods all the way until middle/older age and may play key roles in lifelong maternal health and aging.

Oxytocin and maternal behavior

Despite some making the occasional off-color joke about how some women act different once they enter motherhood, there is no denying that the process of pregnancy and childbirth changes the neurobiology and neuroendocrinology of women. These changes throughout the body and central nervous system are biologically innate to support attention to and nurturing of infants. Neuroplastic changes within the cerebral cortex of the mother may aid in the mother's perception and response to infant cues, such as crying. The ability to recognize such cues is important for giving appropriate care to the infant (Kohl et al., 2018). In recent years, researchers have reviewed experience-dependent changes within the cerebral cortex throughout one's motherhood journey. One hormone in particular, oxytocin, has been studied to gain insight into its role of gating cortical plasticity as well as to explore the mechanisms possibly involved in regulating oxytocin release amid various sensory stimuli (Valtcheva et al., 2018).

Evidence suggests that the emergence of different aspects of maternal behavior evolved to rely on experience-dependent changes that take place in the maternal brain that enable new mothers to process sensory cues from their newborns. While other changes take place, the somatosensory cortex has recently been shown to contribute to parental response in infant sensory cues due to its long-lasting plasticity (Tasaka et al., 2018). While most of the studies that display this phenomenon have been performed in rodents, many scientists believe that there is close translation to the neurobehavior of human parents. Rodents are often used

to study the neural pathways of humans due to rodents being very amenable to the techniques used to selectively monitor and manipulate single cells and neural networks in vivo (Valtcheva et al., 2018).

Oxytocin can selectively gate cortical responses to infant stimuli, and thus facilitate maternal care. This hormone is synthesized in the paraventricular nucleus (PVN) and the supraoptic nucleus (SON) of the hypothalamus, where it deploys its central actions by way of the oxytocin receptor (Figure 3). Its role in mammals involves prosocial functions such as pair bonding in mating, feelings of empathy, and parental care mechanisms, therefore, the priming of cortical circuits in new mothers by oxytocin could lead to further experience-dependent reshaping of neural mechanisms in response to infant cues (Valtcheva et al., 2018). Despite the cortical critical period ending quite early in postnatal development, experience and learning in adulthood can change cortical networks through the brain area's ability to still achieve plasticity. This response evolved due to motherhood being a dramatic natural experience that requires quickly becoming acquainted with infant needs. Because of this, changes in the way infant cues are processed in the sensory cortex are thus a necessary constituent to help support nurturing and support of the new baby (Brecht et al., 2018).

To understand the role of oxytocin in cortical plasticity, it is important to understand which mechanisms might be recruited to change cortical networks involved in behavior change. Long-lasting plasticity in the adult cortex requires subcortical modulatory systems to be activated in a way that can provide behavioral context to incoming stimuli and signals. Particularly in maternal behavior, oxytocin is the main contender for hormonal regulation and modulating neural circuits involved in parenting behaviors (Froemke, 2015). There are two circuit mechanisms complementary to each other that might be engaged in these cortical

networks. First, an infant's needs may increase sensory inputs that drive oxytocin neurons in the hypothalamus directly or indirectly. Having experience-dependent plasticity of oxytocin neurons in the hypothalamus might increase their activity in response to infant stimuli, such as touch or sound, and thus promote peripheral and central release of oxytocin quickly and reliably. Second, having an enhanced oxytocin release could promote cortical plasticity which could increase the detection of infant stimuli. Central oxytocin release from the hypothalamus could also provide a feedforward alteration of cortical activity (Valtcheva et al., 2018).

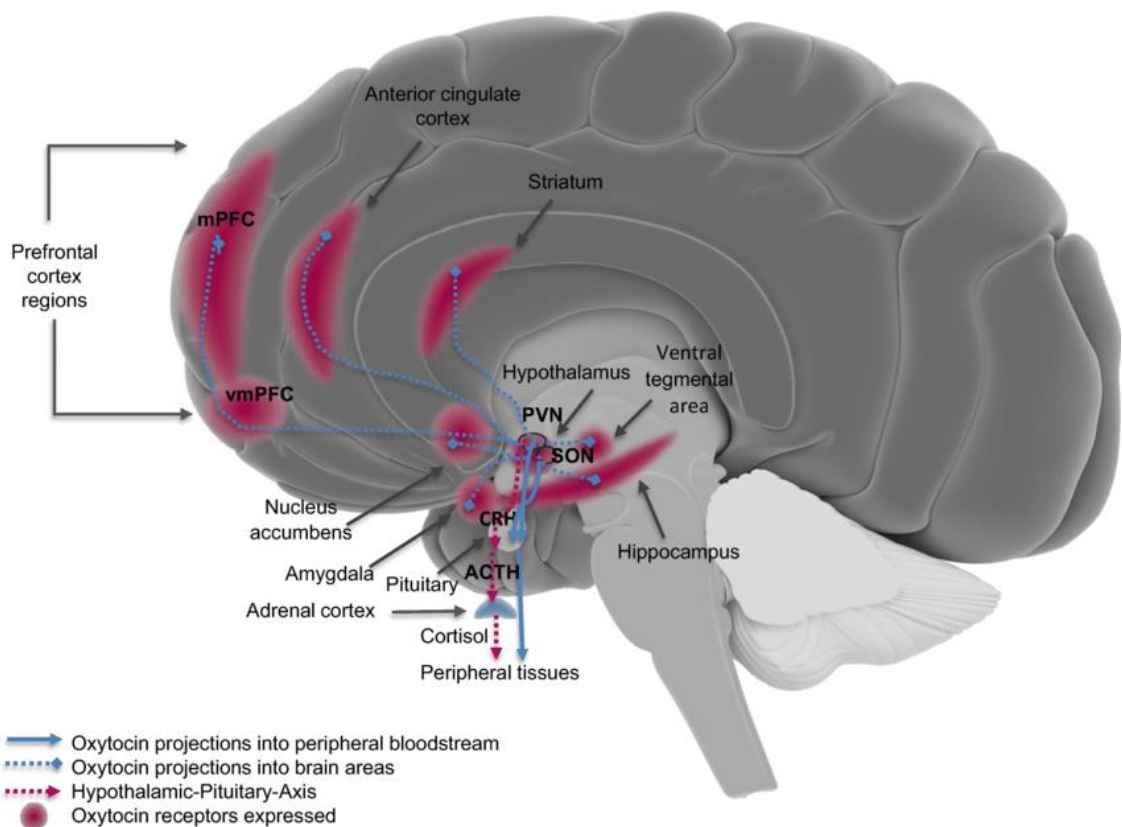


Figure 3. Schematic representation of oxytocinergic projections to mid- and frontal brain areas and the hypothalamic-pituitary axis. PVN, paraventricular nucleus; SON, supraoptic nucleus; CRH, corticotropin-releasing-hormone; ACTH, adreno-cortico-tropic-hormone; (v)mPFC, (ventro)medial prefrontal cortex (Witteveen et al. 2020).

A study out of the Departments of Psychology and Neuroscience at Ohio State University examined whether the medial prefrontal cortex (mPFC) is involved in the network of brain regions regulating behavioral adaptations during the postpartum period for mothers, specifically rats for study purposes. These adaptations include maternal aggression, maternal care, and anxiety. In rats, females who were previously unresponsive or infanticidal towards pups will often engage in a complex range of caregiving activities after parturition, including retrieving misplaced pups back into the nest, nursing or crouching over pups, grooming, and increased aggression towards outside threats (Sabihi et al. 2014). While these behaviors exist to provide and protect the pup, postpartum females also show changes in their emotional states that manifest themselves by increased levels of anxiety-like behaviors. The study age matched adult (9-12 weeks of age) virgin and timed pregnant [gestation day (GD) 14] female Sprague-Dawley rats, and individually housed them in temperature and humidity-controlled rooms maintaining a 12/12 light/dark cycle. The rats had access to food and water ad libitum (Sabihi et al. 2014).

The day of birth for postpartum females was designated as postpartum day 0 (PD0) and each litter was culled to five male and five female pups on PD1. Stages of estrus in virgin females were monitored through daily vaginal swabs which were taken at minimum 2 hours prior to testing. Only virgin females with normal 4–5-day estrous cycles were used for the study. Bilateral infusion of a high specific oxytocin receptor antagonist (OTR-A) was infused into the prelimbic (PL) region of both virgin and postpartum female rats (Sabihi et al. 2014).

On PD3, maternal behavior was assessed when postpartum female rats exhibited high levels of maternal care. Behavioral observations of maternal care included pup retrieval

(gathering stray pups back to the nest), pup directed behaviors excluding retrieval (anogenital or body licking to initiate urination or defecation, nursing, etc.), and self-grooming. Anxiety was assessed in virgin females in diestrus and postpartum females on PD5 when the postpartum females exhibit low levels of anxiety-like behavior. Virgin females were included in this portion of study as a means to examine whether the OTR-A prevented the reduction in anxiety often observed postpartum as well as confirm previous reports that the behavioral effects of OTR blockades are specific to the postpartum period (Sabihi et al., 2014). Maternal aggression was assessed when aggressive behavior seemed to peak on PD7 using the maternal defense test. Mothers were separated from their young and brought into an infusion room while pups were left in the home cage. The postpartum mothers were infused with OTR-A or saline solution and returned to their cages. Twenty minutes after the procedure, a weight matched (± 10 g) female intruder rat was placed into the home cage of the mother. Video recording began once the intruding female was placed into the cage and recorded for 10 minutes. The following behaviors and their associated durations were tested: intruder attacks (lunging and/or wrestling), contact with intruder (following/sniffing intruder), and biting (Sabihi et al., 2014).

The study showed that blocking OTR in the postpartum female's PL mPFC impaired the mother's pup retrieval behavior through increasing time it took to retrieve their first pup. Further analysis showed that postpartum females infused with a lower dose of OTR-A ($0.1\mu\text{g}/\mu\text{l}$) also took longer to retrieve their first pup compared to their saline injected counterparts. Blocking OTR-A in the PL mPFC of postpartum females also enhanced maternal aggression. This was manifested by a decrease in the time elapsed to attack the intruder in the home cage and an increased number in attacks on the intruder. Lower dose

OTR-A (0.1 μ g/ μ l) postpartum females also took less time to attack intruders than the saline controls. Reproductive state and presence of OTR-A infusion into the PL mPFC showed significant effects on anxiety-like behavior in the elevated plus maze (EPM) used to assess anxiety-related behavior within rodent models of study. Postpartum females spent more time in the open arms of the EPM than virgin rats, displaying lower anxiety in postpartum females (Sabihi et al., 2014)

These results displayed further evidence that oxytocin is an important hormone in the repertoire of chemical messengers and neural pathways in mothers. It observed mPFC as a critical part of the oxytocin “maternal circuit” where oxytocin is critical for females to display maternal care behaviors. While mothers infused with OTR-A in the mPFC exhibited impairment within pup directed behaviors, this could be due to oxytocin in the mPFC modulating motivation for other functions within the mPFC, such as attention. Heightened attention could thus lead to greater ability to direct maternal care (Pereira et al., 2011). Despite it seeming contradictory that oxytocin within the mPFC promotes maternal care yet inhibits maternal aggression, the study findings were consistent with the important role oxytocin plays in facilitating pro-social behaviors. To understand this, it is important to understand that maternal care is only in relation to their care of their child, not in relation to fighting off intruders. The nature of the two behaviors are different enough to require two separate neural circuits, thus the pair are affected differently regarding sensitivity toward OTR blockades in the mPFC (Sabihi et al., 2014).

The postpartum period is also a time of reduced anxiety within the mother due to a different endocrinological make-up within the brain and body after childbirth. This was supported within the previous study through postpartum rats spending a greater percentage of

their time in the open arms of the EPM, showing a lower level of anxiety within their surroundings. There is still more work to be done in the future regarding increasing our understanding of the behavioral effects of oxytocin within the maternal brain, as well as the underlying neural circuits coinciding with them. This study was the first to reveal that oxytocin in the maternal mPFC circuit modulates maternal care, aggression, and postpartum anxiety, although the issue is much more complex and requires further investigation into the neural circuits involved (Sabihi et al., 2014). Human mothers especially can utilize this information to gain understanding into how their behavioral changes within the postpartum period evolved to protect their offspring through neuroplastic alterations years after brain development ceases.

Cortisol and Maternal Behavior

Anyone who has become a parent of a child would agree that infant care is often carried out under stressful circumstances. While this care provided to the infant is somewhat linked to the overall aptitude and responsibility of the parenting adult, the overall quality of caretaking behavior is determined by a complex set of factors within the parent-infant relationship itself. These factors include characteristics such as attachment style or a parent's ability to read and understand the behavior of their infant. Perhaps the most critical trait to possess within the early parent-infant relationship is the ability for the caretaker to appropriately respond and react to the infant, even in the most stressful of situations.

Bio-behavioral stress responses are primarily determined by two interacting systems within the brain, the sympathetic nervous system and the hypothalamic-pituitary-adrenocortical (HPA) axis. While the sympathetic nervous system is a fast-acting system within the body involved in regulating specific responses like blood pressure, the HPA axis

performs as a slower-acting system that stimulates the release of the stress hormone, cortisol. In much of the stress research literature today, cortisol has been studied as the primary driver for physiological, behavioral, and cognitive stress within the body (Probst et al., 2017). For breeding mammals, humans included, maintaining a certain level of parental care is necessary to protect their defenseless offspring in life-threatening situations. Considering only females can provide nourishment to infants, they are usually the caretaker more involved in caretaking responsibilities than males are. By acting on “fight-or-flight” reactions often displayed by their male counterparts, females would leave their young vulnerable and unprotected to threats. Rather than a “fight-or-flight” reaction to stress, it has been proposed that females handle stress through a “tend-and-befriend” response (Preston et al., 2013).

To test the effects of stressors on parental behavior, the Institute of Psychology and Center for Cognition, Learning, and Memory at the University of Bern, Switzerland, conducted a study comparing the motivation to show caretaking behavior in stressed healthy young women and men with their caretaking motivation under normal conditions (Probst et al., 2017). In the study, stress was induced in 40 participants, 21 women and 19 men, by use of the cold pressor stress test, with 40 individuals in a control group (22 women, 18 men). The participants rated their urge to care for newborn infants shown on 20 short video clips. There were 10 videos of the infants crying and 10 videos of the infants displaying typical neonatal facial movements and mannerisms. Skin conductance (SC) was obtained throughout the participants viewing of the videos and salivary cortisol was measured as a mechanism to capture response to stress (Probst et al., 2017).

The main finding of the study was that stress-exposed men showed a lower level of caretaking motivation than the control group of men, while women under stressful situations

displayed higher caretaking motivation than women in the non-stressed controls. Similar effects of stress were shown to be sex-specific in the physiological arousal that were brought forth from the infant videos. Stressed men showed much higher SC change than stressed women in response to the infant crying videos. The cold pressor test indicated a comparable cortisol increase within both sexes, however, only men experienced a change in caretaking motivation. Stress had no impact on the modulation of cuteness ratings between the groups (Probst et al., 2017).

III. Motherhood effects on Health and Longevity

In the past five decades, the average maternal age at first childbirth has dramatically increased in the United States even as fertility rates have steadily declined. Studies have continued to examine the associations of maternal age at childbirth and parity with female survival to age 90 and above. The first birth rate of women over 35 years of age has increased by 6-fold in the last half century, with decisions to delay childbearing to further one's education and career playing key roles in the trend (Shadyab et al., 2017). What makes the study of older first-birth age in women unique is that despite the many well-known obstetric complications associated with older maternal age, birth age and longevity outcomes has yet to be extensively studied.

Upon entering motherhood, the mechanisms for why women can show increased and decreased susceptibility to various diseases remain largely unknown, apart from certain types of cancers. Studies have recently suggested that older maternal age at first childbirth is associated with longevity in mothers, however, this association diminishes within women of higher parity (e.g., 3 or more children compared to 1-2 children). One particular theory for this association is that reproductive history is associated with shorter leukocyte telomere length, thus suggesting cellular aging being accelerated (Pollack et al., 2018). Telomeres are regions of repetitive nucleotide sequences associated with specialized proteins at the ends of linear chromosomes in eukaryotic cells. Telomere attrition and a decrease in telomerase activity are both associated with suboptimal immune function, cancer, inflammation, type 2 diabetes, and even Alzheimer's disease. Interestingly, greater amounts of endogenous estrogens commonly observed with lower parity and longer reproductive periods, are also

associated with longer telomere lengths and slower cellular aging because of this (Duarte-Guterman et al., 2019).

Associations between Age at Childbirth and Longevity

A study conducted at Harvard Medical School studied the lifespans of over 120 women born in 1896. This study (Figure 4) compared a group of 78 female centenarians found to be living in the suburbs of Boston with another group of 54 women who died at 73 years of age in 1969. The next-of-kin to these subjects were contacted via the use of data provided by the Massachusetts Registry of Vital Records. The study focused on women with the same birth year of 1896 to minimize issues regarding influences on fertility such as health and contraception-related trends, wars, economic trends, etc. (Perls, 1997).

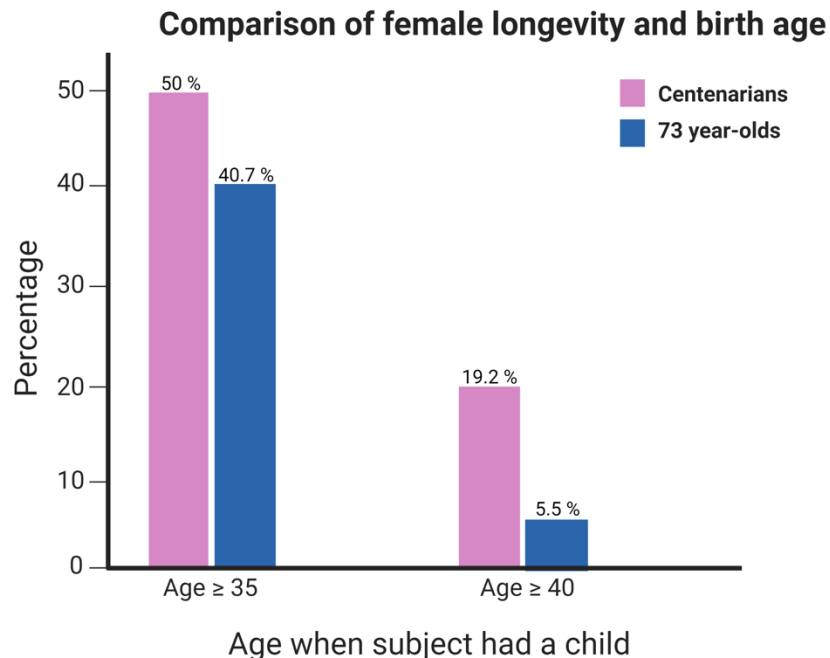


Figure 4. Percentage of women having children at or beyond ages 35 and 40. The difference in the number giving birth at or after age 35 in the two groups was not statistically significant (odds ratio = 1.5, $P = 0.3$), but was significant in those giving birth at or after age 40 (odds ratio = 4.0, $P = 0.02$) (Perls et al., 1997).

During the first quarter of the 20th century, medical science had not advanced enough to provide fertility-enhancing interventions for older women. Due to these circumstances, pregnancy after 40 years of age, and later menopause age, may be associated with extreme longevity in the women studied. Through an evolutionary lens, menopause could act as a protecting mechanism for aging women from the hazards of childbirth (Perls et al., 1997). Therefore, it can be theorized that as humans evolved and began to have longer life expectancies, a woman would eventually reach a point where their survival rate in childbirth would decline due to increased frailty associated with their age. In a similar paper by Rochat et al. written in 1988, the case for menopause evolving could be because “premature death of the mother would also put at risk any existing children and their potential for reproduction” (Rochat, 1988).

Despite menopause continuing to be a biological process all women undergo as they age, lifestyle factors and genes that allow women to age slower continue to have an influence. An analysis of genealogical data from an Old Order Amish community in Lancaster, Pennsylvania shows lifestyle factors that may be associated with increased lifespan. Amish communities are known to be populations with large nuclear families, homogeneous lifestyles, and often keep extensive records of their genealogical history (McArdle, 2006). This analysis was restricted to a group of 2,015 individuals who met three criteria: they had children, were born between 1749 and 1912, and must have survived until at least 50 years old. The study showed that the lifespan of fathers increased in a linear fashion with increasing number of children (0.23 years per additional child; $p = 0.01$), while the mother's life spans increased linearly up to 14 children (0.32 years per additional child; $p = 0.004$) but decreased with each additional child beyond 14 children. In addition, women

with a later age at last birth (>35 years) were associated with a longer life span averaging 3 years longer (McArdle, 2006). This data could suggest that men with high parity and women with later menopause and older age at last birth could be markers for increased lifespan. Nonetheless, it is important to understand the biological and social factors that mediate these relationships, thus potentially providing insight into what factors lead to successful longevity practices.

Others have attempted to study how factors such as race, income, parity, marital status, and education level could play a role in maternal longevity statistics. A case-control study across 311 women who achieved longevity through surviving to the top 5th percentile of their birth cohorts and 151 women in a control group who died at younger ages reported results that women found to have had their last child after age 33 years had twice the odds of achieving longevity than women who stopped having children before the age of 30 (Sun et al., 2015). The one problem with studies like the previous one mentioned is that they are often limited by being designed retrospectively and having relatively small sample sizes of women achieving longevity. In addition, the Sun et al. 2015 paper failed to factor age at first childbirth, a factor potentially more important from the perspective of public health.

To fix some of the flaws in previous studies, the Women's Health Initiative published a paper in the *American Journal of Public Health* (Shadyab et al., 2017) following a cohort of 20,248 postmenopausal women in the US recruited between 1993 and 1998 until 2014 when the study concluded. These women had an average age of 74.6 years at the start of the study and were followed for up to 21 years. At baseline, women with older ages at first birth were more likely to have graduated college, to be married, had higher incomes, and were less likely to have chronic illnesses such as obesity or diabetes. These women also were found to

have entered menopause at older ages and typically had only 1 term pregnancy in their lifetime. On the contrary, women having had 5 or more pregnancies were less likely to have graduated college, while being more likely to have chronic diseases, obesity, and low income. Women with 5 or more children often had never used hormone therapy for birth control, were younger at first childbirth, and were older at their last pregnancy or childbirth and older entering menopause (Shadyab et al., 2017).

During follow-ups with the cohort of women, results showed a total of 10,909 (54%) women had lived to 90 year of age or above, thus being categorized as reaching “longevity.” In the fully adjusted results model, the linear trend was found to be significant toward higher odds of longevity in women with later ages of their first childbirth (p for trend = 0.04). When comparing women who had their last child before 25 years old, there was no significant difference in odds of achieving longevity than women who had their last child much older (p for trend = 0.27). These associations regarding age at first and last child with longevity did not vary by race, parity, or income differences (Shadyab et al., 2017).

Associations between later age at first childbirth and longevity may be explained by many factors. The ability for a woman to deliver a term infant at an older age may also be an indicator that the woman will be older at natural menopause (Crawford, 2015). Women who experience natural menopause at an older age may be more likely to have longer lifespans, which could be explained by their overall health being better due to lifestyle factors. For purpose of example, women who experience menopause later have been found to have better nutrition and less stress which could be linked to overall greater socioeconomic status during childhood (Crawford, 2015). The findings of the *Women’s Health Initiative* paper, however, were independent of menopausal age. In addition, older maternal ages have increased risk for

obstetric complications such as gestational diabetes and hypertension. Maternal mortality risk also increases with age across all demographics and races.

Potential weaknesses within this study include a lack of information about the women's family history of achieving longevity or whether pregnancies were able to be achieved by modern reproductive technology. Study findings were very similar even after excluding women who reported having difficulties becoming pregnant. Strengths of the study include long-term follow-up with the women, high retention rate of the women across the study timeline, a multiethnic study cohort and many women achieving the longevity classified age of over 90 years old (Shadyab et al., 2017).

The Gillings School of Global Public Health Department of Epidemiology at the University of North Carolina at Chapel Hill conducted a cross-sectional analysis of 1,232 women from the National Health and Nutrition Survey seeking to examine maternal age at last birth and telomere length. This survey was conducted between 1999 and 2002. Both perimenopausal and postmenopausal women aged 40 years and older were included. The maternal age the woman's last live birth was self-reported within the survey, and leukocyte telomere length was measured through using qualitative polymerase chain reaction (PCR) (Latour et al., 2020).

The results of this study indicated that later maternal age at last birth was associated with longer leukocyte telomere length in both perimenopausal and postmenopausal women. Some evidence suggested that the association may be slightly modified by the number of live births a woman undergoes or their use of oral contraception, such that the association holds only among women with 1 or 2 live births and women with a history of never using oral contraception (Latour et al., 2020). Nonetheless, these results could have effects on the long-

term health of a population. An example of this is cell division, and a small portion of telomeric DNA being lost with each cell division. As telomeric length reaches a critical limit, the cell undergoes apoptosis or cellular death. Therefore, telomere length can perhaps serve as a biological clock used to determine lifespan of the cell and the organism at large (Shammas, 2012). If later age of last childbirth is associated with longer leukocyte telomeric length, this could be an indicator for longer overall lifespan of the woman.

Fetal Microchimerism and Mothers

Fetal microchimerism, the phenomenon that fetal cells persist in mothers for decades after their delivery, have been recently studied to determine what kinds of outcomes could facilitate from the presence of these cells. These persistent fetal cells were first found to be implicated in autoimmune diseases of the mother, however, parallel studies in both human and animal populations have recently suggested that microchimeric fetal cells may play healing or reparation roles in the response to tissue injury. Adult skin injury requires a specific sequence of events in order to “patch” the defect caused by said injury. All three phases of wound healing – inflammation, tissue formation, and tissue remodeling – must occur for repair to full take place. Within six to twelve months following acute injury to an area, main type 3 collagen to type 1 collagen remodels the extracellular matrix. Nonetheless, the healed would never regains the properties of uninjured skin. Researchers blame this occurrence on angiogenesis, inflammatory responses, and the decline of fibroblast function in adults (Mahmood et al., 2014). Conversely, the skin wounds of early-stage mammalian embryos can heal without the formation of a scar and completely restore the original skin architecture. This may be linked to greater cytokine and growth factor profiles within embryos (Mahmood et al., 2014).

Pregnancy is full of events that not only affect the health of the child into adulthood, but also phenomena that may have lasting health implications for the mother. Passage of fetal cells into maternal circulation is one such phenomena. These fetal cells latch onto maternal tissues throughout and after pregnancy and continue to persist within the mother for decades within the bone marrow and organs, becoming microchimeric cells. Previous studies suggested that this presence of fetal cells could cause tissue injury in the mother. Large populations of fetal skin cells have been found present in women presenting with polymorphic eruption of pregnancy, an inflammatory disease in the skin during pregnancy. Biopsies of these areas have confirmed that fetal cells are significantly more frequent in inflamed tissue areas than healthy skin (Nassar et al., 2012).

With adult bone marrow being a key site for pluripotent stem cells, it is a plausible hypothesis that engrafted microchimeric fetal stem cells found within the bone marrow of mothers to sites of skin injury could be coupled to endogenous stem cell populations for more efficient and beneficial healing process. It is still a rather controversial topic, nonetheless, there is potential for controlling the delivery systems of fetal cells to skin injury to promote healing due to fetal cells being differentiated cells possessing high expansion, regeneration, and lower immunogenic properties (Applegate et al., 2009). With the rise in use of the cesarean section (CS) as a surgical procedure for pregnant women, many deliveries have become safer due to the procedures ability to offset vaginal delivery risks, and its ability to be electively scheduled. Despite this, CS scarring and complications have imposed burdens on women post procedure in both economical and psychological aspects. What makes this scarring from CS beneficial to research is that it creates the optimal tissue conditions to study associations between wound healing and fetal cell presence in the wound.

Through gaining understanding from CS scarring, strategies may be found to implement towards other tissue scarring to manipulate adult healing towards more fetal-like conditions (Mahmood et al., 2014).

A study out of the Department of Obstetrics and Gynecology at the Anu Research Center in Cork, Ireland, hypothesized that wound healing in women becomes more fetal-like after pregnancy, and that this healing may be due to transplacental trafficking of microchimeric fetal cells containing regenerative capacities (Mahmood et al., 2014). The aims of the study were to show the presence of microchimeric fetal cells in maternal tissue injury sites and demonstrate their contribution to tissue repair. 70 skin biopsies, containing 31 normal (unwounded) skin samples from first CS and 39 CS scars were harvested during the surgical procedure. The women were grouped into 3 cohorts based on their reproductive history. Their groups were women without miscarriages, women with previous miscarriages, and normal skin/uninjured skin controls. The women were all in their early 30s, and never had a transfusion or organ transplant.

The results of the study demonstrated the presence of male cells of presumed fetal origin in the CS scars of parous women, thus implicating their role in the healing process after the CS. XY fluorescence in SITU hybridization (FISH) analysis identified male cells in CS scars of women with first male pregnancy delivered by CS but not from women in the control group. Some CS scars from women with no sons displayed male cells, as many women displaying male cells with no male son had experienced a miscarriage of unknown gender. The study suggested that injury of skin at CS surgical sites (Figure 5) recruits more fetal cells to aid in the regenerative process of healing. Fetal cells found elsewhere is likely

due to random distribution of these cells throughout the body after pregnancy (Nassar et al., 2012; Mahmood et al., 2014).

Male cells of presumed fetal origin were seen as isolated single cells within the epidermis throughout this specific study. They were never observed to be in clusters. Fetal cells present within the maternal epidermis were identified morphologically as keratinocytes by their round vesicular nuclei and epithelial cell morphology. Fetal cells stained positive for Cytokeratin, indicating these cells differentiated into the local skin cells. Compared to previous studies, this study found a higher frequency of engrafted fetal cells as keratinocytes up to 8 years after CS. This may indicate the fetal cells being self-renewing stem cells (Mahmood et al., 2014).

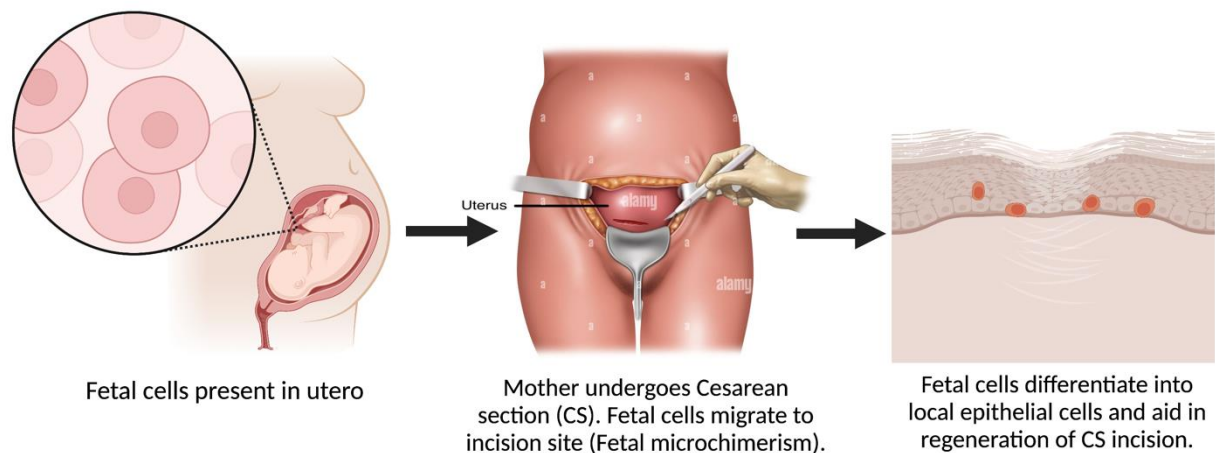


Figure 5. Fetal cell migration through cesarean section (CS) incision site may be involved in tissue repair.

Through this self-renewing capacity and long-term potential of persisting fetal stem cells to form undifferentiated cell lineages, this regenerative capacity may confer to females an advantage in terms of long-term health and longevity. Perhaps fetal cells not only have

potential implications for women immediately after giving birth, but also many years post-pregnancy and beyond. Studies such as this one open doors for possible future research on how fetal cell transplantation could benefit wound healing, inflammation in the body, and angiogenesis in those who lack vascular integrity, such as diabetics. Research into new stem cell therapies could start by ferrying off fetal cell research and investigate how this work can be furthered or made mainstream.

The Influence of Parity on Brain Disorders and Strokes

Due to the dramatic influx of hormonal changes associated with maternity, women can sometimes become more susceptible to various diseases or disorders. Starting within the perinatal period, approximately ranging from conception to 18-24 months after the birth of the child, women exhibit greater risk for developing affective disorders such as anxiety or depression. Approximately 15% of women will experience postpartum depression, and 8% will experience anxiety-related disorders following the arrival of the baby (*The Lancet Psychiatry*, 2015). Certain amounts of parity are also positively associated with an increased risk of developing Alzheimer's disease (AD). Studies have found that having more than five completed pregnancies increases one's risk of developing Alzheimer's disease, while contrarily having an incomplete pregnancy may reduce one's risk of developing Alzheimer's disease (Jang et al., 2018). Additionally, the study found that in women without dementia, incomplete pregnancies may increase memory scores relative to women who never have experienced incomplete pregnancies. This finding suggests that there may be an association between incomplete pregnancies and reduced cognitive impairment with aging (Jang et al., 2018). However, previous studies failed to find this same association between parity and risk of developing AD, which may be due to genotype differences.

Other genetic factors would have to play a role in one's susceptibility in an AD diagnosis due to the disease being caused by protein misfolding and buildup within the brain. A study out of the Institute of Molecular Biology and Genetics at University La Sapienza in Rome, Italy, studied how certain genetic factors may be associated with parity and AD risk (Corbo et al., 2007). The study focused on apolipoprotein E (APOE), and how the $\epsilon 4$ allele of the protein can be a major genetic risk factor for AD. The $\epsilon 4$ allele is known to reduce the age of AD onset and interact with the parity of a woman to influence AD onset age. The study involved determining APOE genotypes of a sample of 176 women with sporadic AD throughout the sample. The parity of each woman was recorded (Corbo et al., 2007).

Results from the study compared a APOE genotype distribution in both parous and nulliparous AD women, confirming that the APOE $\epsilon 3/\epsilon 3$ genotype is associated with higher fertility and the $\epsilon 4$ -carrying genotype being associated with lower fertility. Through analyzing the combined effects of fertility and one's APOE genotype, parity was found to be associated with a significantly lower AD onset age (73.8 \pm 6.2 years) than nulliparity (80.7 \pm 5.0 years; $p = 0.0007$) among test subjects with $\epsilon 3/\epsilon 3$ genotypes and $\epsilon 3/\epsilon 2$ genotypes. These results were not found in women who were $\epsilon 4$ carriers, which suggested that nulliparity may be protective against developing AD in non- $\epsilon 4$ genotype carriers (Corbo et al., 2007). On account of these results, it may be a worthwhile pursuit for future studies to examine how factors such as genotype and parity amount can interact among each other to affect health outcomes later in life for mothers.

It is also a common phenomenon that increased parity is also often associated with obesity and excessive weight gain. In addition, higher risk of cardiovascular disease and stroke is particularly detected in women who have experienced pregnancy complications

including preeclampsia or gestational diabetes (Hauspurg et al., 2018). Within animal models of mice, it has been found that parity improves stroke outcomes in middle age, but also increases mouse body weight, reduces activity level, and impairs bodily energy homeostasis after weaning pups. Parity has been shown reducing estradiol levels across estrous cycles of women, thus suggesting that parity's protective effect on stroke brain injury might be due to lower estradiol levels than nulliparous counterparts. With dementia and AD being previously linked to diabetes, stroke, obesity, and cardiovascular diseases, it makes sense to also observe effects of parity on the outcomes of these diseases as well. Because of this, it may create the need for future treatment to be tailored to the patient based on sex, genetic factors, and reproductive history in order to best treat the patient.

IV. “Dad Genes”

Despite their role in the reproductive process only involving the fertilization of the female egg, fathers are not let off the hook when it comes to the biological changes that take place after becoming a parent. Humans have mostly co-parented throughout world history, which opens the ability for males to be susceptible to the neurological and biological changes that take place in parenthood. One of the most stereotypical physical changes associated with becoming a father is the “dad bod” where new fathers tend to gain some unwanted weight in the months and years following a child being born. From a cultural perspective, this term “dad bod” is another way to poke fun at new fathers for not being as cool or culturally up to date as they once were (Garfield et al., 2016). This phenomenon could be associated with a variety of factors happening within the biology of men entering fatherhood, including the endocrinology and neurochemistry of men changing once an infant is placed into their life (Gettler et al., 2012).

Prolactin

Among mammals, humans are unusual in the fact that fathers often provide an intense amount of care throughout the childhood of their offspring. Perhaps due to this anomaly, research has been conducted to study the hormonal architecture involved in the regulation of paternal investment in humans. One of the hormones responsible for reproductive functions in both males and females is prolactin, a heavily studied hormone in relation to females but often overlooked concerning male behavior (Gettler et al., 2012). In females, prolactin is best known for its role in lactation and nurturing the child through breastfeeding.

In a study by Stölting and Wilson, males in seahorse species responsible for incubating eggs within their bodies require elevated prolactin production for brooding pouch

health and optimal embryonic development (Stölting & Wilson, 2007). Studies such as this one has led scientists to believe that prolactin is associated with an increased paternal investment in human populations, as well as some of the associated weight gain that fathers undergo. While there has been a variety of animal studies showing prolactin levels to be elevated during periods of caring for offspring in certain animal species, evidence for this phenomenon in humans is difficult to pinpoint due to its complexity.

A study by researchers at Northwestern University sought out to determine if there is evidence for prolactin levels playing a role in human paternal behavior. A sample of 289 men, age 21-23 at baseline, were studied from Metropolitan Cebu City, Philippines to evaluate the relationship between prolactin and various components of reproductive behavior and relationship status. Among those in the sample, results showed fathers having higher prolactin than nonfathers ($P = 0.006$), as well as fathers of young children displaying higher prolactin levels than fathers with older children ($P = 0.050$). Among the population of nonfathers, men displaying greater baseline prolactin reported having more lifetime sexual partners as well as more sexually activity in the month before sampling (Gettler et al., 2012). This finding makes the issue of prolactin levels a bit more complex than originally hypothesized and creates an avenue for future study. Despite the complexity of all factors affecting prolactin levels, the study found that fathers in committed romantic relationships displayed the highest prolactin baseline, with significant differences when compared to single nonfathers and childless men not residing with a partner. The behavioral variation associated with prolactin is based on a man's parental and romantic status but may also occur from complex endocrinological interactions with other hormones or neurotransmitters, including,

but not limited to testosterone, estrogen, dopamine, serotonin, oxytocin, and the neural circuits associated with each (Gettler et al., 2012).

Fatherhood and Weight Gain:

To study the correlation between fatherhood and weight gain, a 20-year longitudinal study by Garfield et al. was published in the *American Journal of Men's Health* during 2016. This group of researchers sought to follow body mass index (BMI) trends in young males during their transition from adolescence into fatherhood in a nationally representative sample. The study considered minority community sizes and used a wide range of starting BMIs to create the most accurate study possible (Garfield, 2016). Height and weight measurements were collected throughout all four waves of the study: Wave I ($n = 10,263$ males, ages = 12-21 years) in 1994 to 1995; Wave II ($n = 7,192$, ages = 13-21 years) in 1996; Wave III ($n = 7,192$, ages 18-28), six years later in 2001 and 2002, and Wave IV ($n = 7,347$, ages = 25-34 years) six years after in 2007 to 2008 (Garfield, 2016). Height and weight data were self-reported in Wave I and measured by the interviewer in all other subsequent waves of the study.

Researchers intentionally oversampled adolescence from various economic and racial/ethnic subgroups to buffer against nonresponse and attrition in an attempt to allow the sample to be as representative of the adolescent population as possible (Garfield, 2016). The fatherhood status of the subjects was divided into three categories: resident fathers, nonresident fathers, and nonfathers. This classification was held constant through all future waves, and nonfathers were the referent group for analyses. To aid in the simplicity of comparisons of changes in both fathers and nonfathers, the term “fatherhood years” was used as the unit of time for the study. Of the 10,253 men included in the study, 6,828 (66.5%)

were nonfathers, while 3,425 (33.5%) were fathers by the end of Wave IV study and sampling. Of the sample, 20.03% were nonresident fathers, while 79.97% were resident at the time of the child's birth. Marriage varied most significantly in the study, with 78% of resident fathers being married compared with 8% nonresident fathers and 13% nonfathers (Garfield, 2016).

In male BMI trajectory, age is known to play a significant role in the positive association between BMI over all fatherhood years for all young men. Any changes in BMI for nonfathers in the study was due solely to age. Figure 6 reveals comparison between resident and nonresident fathers with nonfathers, displaying different BMI trajectories based on the fatherhood status of the man. The study even suggests that "while all young men's BMI changes over time, the way it changes is contingent on fatherhood status and whether they become nonresident or resident fathers" (Garfield, 2016). The young men who would later become nonresident fathers showed a decrease in BMI when compared with nonfathers in the pre-fatherhood period (Figure 6). Income, marriage, and screen hours each day were all positively associated with a higher BMI.

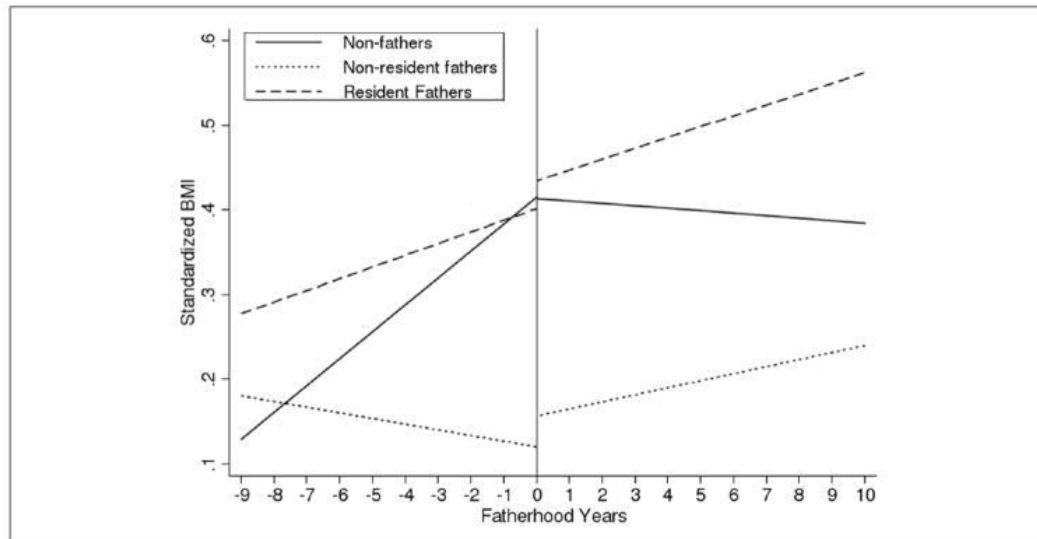


Figure 6. Predicted standardized body mass index (BMI) levels before and after entrance into fatherhood (Garfield, 2016).

When looking for explanations as to why fatherhood is positively associated with an increase in one's BMI, the reasoning for the occurrence is multidimensional. The BMI males have in adolescence and early adulthood is known to set the course for much of adulthood and is often difficult to deviate from. Earlier studies focused on male BMI have been historically aimed at increased heart, cancer, metabolic, and death risk, though few have accounted for the common male milestone of becoming a father (Garfield et al., 2016). The biological changes men undergo after becoming a father cannot be ignored when aiming to fully understand why BMI and fatherhood are so closely intertwined. One of the most recognized biomarkers found in new fathers is a sudden and drastic drop in overall testosterone levels (Gettler, 2011).

It is important to focus on establishing preventative measures to keep fathers from becoming obese due to the influence of a fathers' weight on children's weight outcomes. Analyses have been conducted showing how in families with an overweight father and a normal weight mother, their odds of having an obese child within the next 4-5 years were

4.18 times greater than the odds of two normal weight parents. It is however necessary to establish that having a normal weight father and an overweight/obese mother does not provide indications that one's child would experience childhood obesity (Freeman et al., 2012). Paternal behaviors also influence a child's risk of experiencing obesity more than maternal behaviors. In 2013, the Centers for Disease Control and Prevention reported 96% of resident fathers and 30% of nonresident fathers ate at meal with their <5-year-old child either every day or multiple times per week, thus showing the vast opportunity for a father to influence their child's dietary habits (Jones & Mosher, 2013). Within the last decade, the Healthy Dads, Healthy Kids program showed significant results in promoting weight loss and improving health-related outcomes in fathers and improving eating habits and physical activity statistics among children. Furthermore, it is an important measure to target fathers while they are amid this important developmental stage of fatherhood as it may be a beneficial approach towards improving the health and wellbeing of both fathers and children alike.

Testosterone and Cortisol:

Through humans coparenting throughout world history, hormone fluctuation occurs after having offspring as the body's way to prepare for the upcoming period of caring for the new child. Even outside of *homo sapiens*, species that have males caring for their young experience fluctuation within their testosterone levels throughout the reproductive process. Testosterone is often high during the mating period for animals, only to later decline to allow for males to provide caregiving to their new offspring. In male mammals, humans included, testosterone is responsible for stimulating the development and maintenance of traits and behaviors involved in reproduction, including muscle mass, aggressivity, sex drive, and

indicators of courtship. In a 2011 study by Gettler et al., a large representative study was performed in the Philippines that showed that men with high waking testosterone were the most likely males to become partnered fathers by the time the 4.5-year study concluded. The conclusion of the study also revealed that the men who became partnered fathers experienced larger declines in waking and evening testosterone that were significantly greater than the testosterone declines found in single nonfathers, with a P-value of <0.001 . Remaining consistent with the hypothesis that child interaction suppresses a man's testosterone, fathers that reported 3+ hours of childcare daily were found to have lower testosterone levels at follow-up when compared to fathers not involved in their child's care (Gettler, 2011).

As mentioned previously in relation to prolactin, the biology of parental involvement is a rather complex issue that one singular metric cannot fully describe. Regarding hormones, questions of whether basal and/or reactivity measures can predict different aspects of parenting remain unclear. A study out of Notre Dame University (Kuo et al. 2018) examined testosterone (T) and cortisol in men, their changes, and its involvement in men providing childcare and play with their newborn. The study followed a sample size of 298 fathers whose partners gave birth at a UNICEF-designated "baby-friendly" hospital. These facilities encourage fathers to hold their newborn child within 1 hour of birth, following the chance for mothers to engage in skin-to-skin bonding time. Researchers measured the fathers' salivary T and CORT levels before and after the holding of their infants. The analysis (Table 1) included both basal and short-term CORT and T changes. In the following 2-4 months after the couple's hospital stay, the fathers were contacted to complete a questionnaire discussing involvement with childcare (Kuo et al., 2018).

Results of the study showed CORT levels of fathers decreased during the time they engaged in holding their newborn in the hospital. Both basal and reactivity CORT level could be used as a predictor of fathers' involvement in childcare and play months after birth. In addition, fathers' basal T in the postnatal period immediately after birth was a predictor of greater childcare involvement in the months following (Kuo et al. 2018).

Variable	Direct	Indirect	Play
Birth day basal T	-0.04	0.15	0.17
T change during holding	0.14	0.07	0.03
Birth day basal CORT	0.25*	0.25*	0.27*
CORT change during holding	0.20	0.31**	0.26
Control basal T	-0.28**	-0.33**	-0.14
Control basal CORT	0.18	0.25*	0.13
Parity ^a	-0.34***	0.00	-0.19*
Marital status ^b	-0.04	-0.27**	-0.05
Fathers' age	-0.17	0.03	-0.08
Infant's sex ^c	-0.01	-0.10	-0.22**
R-squared	0.35***	0.26***	0.27***

Table 1. Multivariate regression models predicting fathers' post-partum involvement from measures of testosterone (T) and cortisol (CORT). *Note:* Standardized coefficients presented. ^A Parity, 0 = first-time father, 1 = experienced father. ^B Marital status, 0 = unmarried, 1 = married. ^C Infant's sex, 0 = female, 1 = male. * $p < .05$. ** $p < .01$. *** $p < .001$.

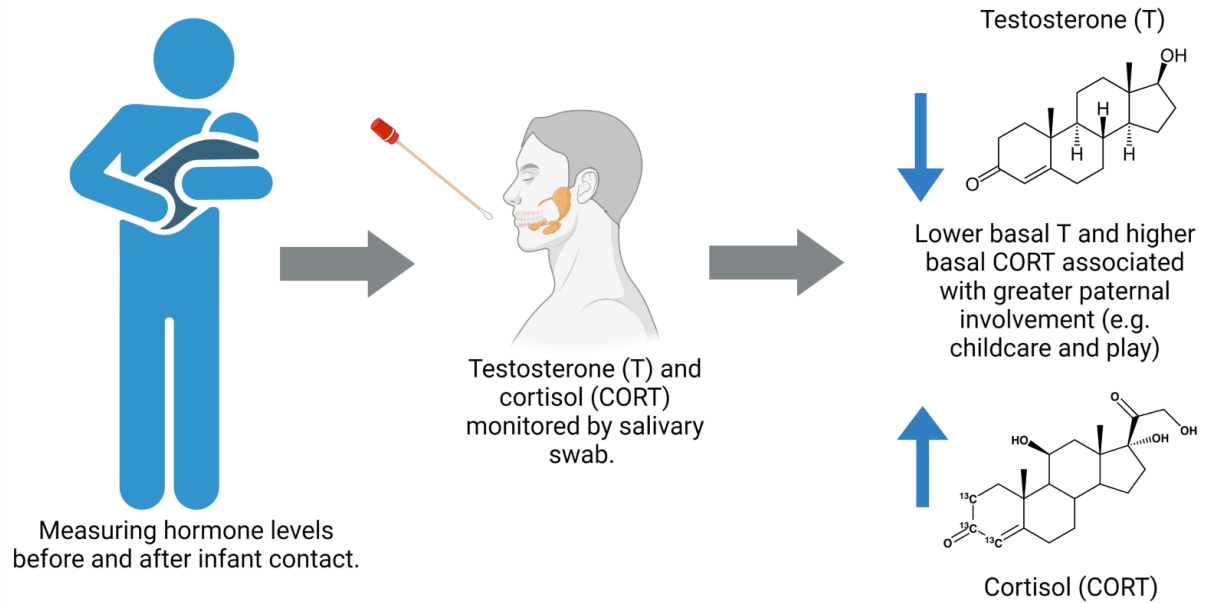


Figure 7. Lower basal testosterone and higher basal cortisol levels are associated with increased paternal investment.

Basal T measures on the control day, rather than the day of birth, were predictive of a variety of involvement types (Figure 7). Fathers displaying lower basal T on the control day later reported engaging in more direct and indirect care when followed-up with. A similar relationship was not observed however for fathers' play, an activity often considered to be much more pleasurable than activities such as doing the child's laundry or changing their diapers. Basal T on the birth date of the child was not statistically significant in predicting later paternal involvement at follow-up. T levels on day of the infant's birth was a potential representation of atypical levels due to the witnessing of the infant's birth rather than a true basal level. Levels of T during momentous occasions are often not a good representation of typical baseline T levels on a normal day-to-day basis. These results suggest that reduced basal testosterone may be linked with an enhanced level of indirect and direct parenting effort from fathers in the future months (Kuo et al., 2018).

Basal CORT of fathers on infant's birth date was predictive of later paternal involvement across various dimensions, with higher basal CORT being predictive of heightened paternal involvement in following months. differing from birth date T. One hypothesis for this happening is due to CORT being elevated in fathers as a survival mechanism to focus men's attention on increasing parenting effort (Kuo et al., 2018). This would complement previous work showing CORT elevation association with greater expression maternal behaviors during first months of the infant's life (Mileva-Seitz et al. 2010). The results of these studies show the potential relevance to further explore paternal neuroendocrinology in the future to solidify some of these theoretical models associated with hormones and paternal behavior.

Longitudinal evidence has been collected that concludes that men who are husbands and fathers typically display lower T levels than their unmarried or nulliparous counterparts. Men with elevated T are often thought to more frequently pursue status-seeking, risk taking, and competitive behaviors that may increase opportunity for mating, however, studies continue to suggest that such behaviors could be incompatible with specific aspects of parenting and romantic commitment long-term (Gettler et al., 2013). For example, among the US military population, men with higher T levels commit more infidelity and experience more frequent marital disruption than their lower T counterparts. Higher T men also have greater trouble experiencing sensitivity to infant cries whenever they become fathers (Fleming et al., 2002). In contrast, fathers with lower T often more frequently engage in caretaking behaviors, with some studies suggesting that a man's T rapidly declines in response to them expressing nurturing behaviors or directly interact with their children (van Anders et al., 2013).

V. Conclusion

Upon surveying the vast wealth of knowledge regarding biological changes that take place when one enters parenthood, one can both respect the biology of parenthood and seek to develop protocols for how one can modulate such behaviors and changes to best benefit parents. Neuroscientists have been mapping both maternal and paternal brains in response to infant stimuli for some years now. Through using non-invasive and sensitive techniques such as the functional magnetic resonance imaging (fMRI) in parenting research, many discoveries have been made that add to the knowledge of the brain at the basis of parental activity. Studies have physiologically confirmed that the maternal brain reflects a multitude of behaviors, with brain scans often displaying a discrete maternal brain activation occurring in relation to each certain aspect of such behavior. What makes this research have a real-world impact is that through recording these changes in brain activation in response to infant stimuli, these changes can be used as potential biomarkers for the development of new diagnostic treatment strategies for parents at-risk for mental disorders associated with new parenthood.

Recent brain imaging studies have provided many examples of how this imaging can identify certain changes in behaviors through neuronal activation. For example, during subconscious processing of fearful faces, amygdala activation and connectivity has been found to significantly increase (Swain et al., 2014). During this, an fMRI may be able to provide insight into the neurological basis of subconscious parental responses that one may feel “happens naturally” rather than making a subconscious decision to act on the behavior. In addition, certain behavioral measures of emotional function such as counseling or therapy may be insensitive to the intricacies of the biology underneath the behavior. By using fMRI,

important biomarkers of behavioral measures can now be used to diagnose psychopathology and treat specific brain areas like the amygdala for disorders such as depression or panic disorder associated with parenting; therefore, imaging data collected can complement behavioral information gathered from counselors or therapists (Swain et al., 2014).

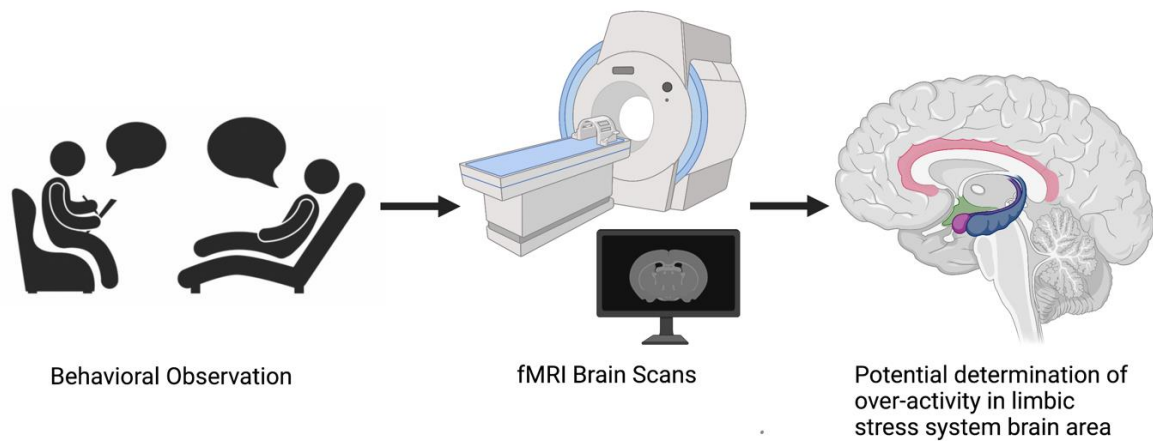


Figure 8. Behavioral observation paired to brain imaging may lead to determination of specific mechanisms that modulate parental behaviors.

In a distressed new mother, observational information can be gathered to answer questions such as whether a parent is at risk of providing poor maternal care or may have an inability to provide sensitivity necessary to care for the infant, thus showing potential biases in her neurological attention systems. Through joining brain imaging to behavioral therapy findings, a better understanding of mechanistic specificity can be obtained that may be used in the future to provide more nuanced drug therapies to assist parents who are more likely to experience anxiety or depression after the arrival of the child. If one can find impaired behavioral performance in a parent under stress, imaging could be used to determine if this stress is due to over-activity in limbic stress systems or because of underactive prefrontal control systems within the brain. Gathering more information on which neural mechanisms are responsible for driving specific behavioral outcomes has important implications in future

treatment designs for at-risk parents (Figure 8). These interventions could be behavioral or drug therapies, nonetheless, the treatments would focus on reducing stress responses, improving executive brain function, or both (Schilbach et al., 2013).

Finally, understanding biological phenomena that occur within males upon becoming a father may provide benefits through this information leading to protocols that can benefit the biology of future generations of parents. Understanding how new fathers are predisposed to heavy depletions of sex hormones opens the possibility for study on protocols to prevent such a drastic hormone decrease that can lead to obesity and other health outcomes. Other hormonal mechanisms require further study to fully understand how endocrinology combines with neurology to complete the full picture of paternal biological changes affecting health and mental wellbeing of fathers worldwide.

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