Deepening the nature v. nurture debate: How hormones impact development in the womb is often most key

One of the longest-running debates in the realm of child development is the question of whether we are the result of our environment or our genetics. Reality, however, is more complex and more intriguing.

The oversimplification of this matter, which has been a major topic of debate and scientific inquiry among psychologists, physicians, and scientists of all stripes since the term nature vs. nurture was coined by Francis Galton in 1869, does not give due consideration to that time when the two are inextricably intertwined: that crucial forty weeks, give or take, during which a human grows from fertilized egg to embryo to fetus. And there is now research suggesting a third manner of passing on genetics to offspring: the control of genetic expression and hormonal imprinting set in motion by exposure to hormones during gestation.

The research in this arena is ongoing, but it is clear that hormones released during gestation appear to affect the development of the fetal brain in a number of ways.

It is common knowledge that deficiencies of nutrients in a pregnant person's diet, pathogens, medications, and other outside influences can have a teratogenic effect. For example, a medication used to treat severe cases of cystic acne, Acutane (retinoic acid), is known to cause birth defects through mutation of the SSH Gene(Sonic Hedgehog Gene).

What is not well known outside the scientific community is that factors within the gestational partnership between fetus and parent, in particular the balance of hormones released into the mother's bloodstream, also have a profound effect on the expression of genes within the placenta and the fetal brain, affecting intelligence, mental health, social and developmental disorder manifestation, brain size and structure, susceptibility to stress and sensitivity of the fight or flight response, and hormonal imprinting, to name a few.

The mother's hormones appear to have a programming effect on the fetal brain through the phenomenon of hormonal imprinting. The exposure of the developing brain to varying levels of particular hormones will permanently set how responsive the fetus's hormone receptors are for the rest of their lives. Two such examples of hormonal imprinting involve oxytocin and cortisol.

Exposure to cortisol while in utero appears to affect the formation of the stress-response axis, responsible for how the offspring reacts when exposed to stressful stimuli. But it isn't as simple as a dose-response system or the negative effect of teratogens(an element that causing malformations of an embryo or fetus by way of exposure).

When examining cortisol exposure during pregnancy, it appears that timing of exposure, amount of exposure, and the slope of increase in exposure(cortisol exposure naturally increases over the course of a pregnancy) all contribute to the final outcome. What we find is a U-shaped curve where the lowest and highest levels of cortisol exposure in pregnancy are associated with negative outcomes, including

exaggerated stress response in childhood and impaired brain development.

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As evidenced by a study published in 2010 involving 125 full term infants whose mothers were tested for cortisol levels and surveyed for psychological states five times during pregnancy, early exposure to elevated cortisol levels negatively impact offspring while late exposure to high cortisol has a salutary effect. The infants in the study exposed to elevated cortisol early in gestation showed slower growth and lower scores in mental development when tested at 12 months with the Bayley Scale of Infant Development(BSID) whereas infants exposed to higher cortisol during late gestation showed faster development and higher mental development scores on the BSID.

It also appears that a steeper increase in cortisol across the course of a pregnancy, starting with a lower level in the first trimester and ending with a higher level in the last few weeks, improves outcomes evidenced by faster mental development over the first year and resulting in higher intelligence scores at a year. Only infants with a moderate average exposure (lack of either high exposure in the first 18 weeks, no abnormally high exposure at any recorded time and a moderate level recorded overall) to cortisol do not exhibit an exaggerated stress response in infancy. A study conducted in India, in which 133 pregnant women were evaluated for depression before and after birth using the Kessler scale and the Edinburgh Postnatal Depression Scale and then following up with 58 of their infants, looking for a connection between cortisol secretion during pregnancy and exaggerated stress responses in childhood found that two-month-old infants tested for salivary cortisol levels following immunization showed exaggerated responses to immunization if they had been exposed to very high or very low levels of cortisol during pregnancy.

The implications of these findings are many and in need of further research, but thus far it appears that increasing cortisol exposure once the developing child has passed the vulnerable first trimester of development provides a blueprint within the brain for future stress responses in life — stress responses that should approximate those needed for survival in the world the parents are living in. It stands to reason that a child born into a high-stress world (threat of natural disaster, war, or predators) would need a

sensitive and rapid stress reaction to survive. In theory, by exposing a fetus to high levels of cortisol early in pregnancy, we create a child built for extreme reactions to meet an extreme world. When the developing child is exposed to unusually low levels of cortisol in the womb, their stress-response axis may be unable to properly process stressors (cortisol); when tested in infancy, this is evidenced by an exaggerated response to stressors, similar to their high cortisol exposure counterparts. This line of thinking leads us to the hypothesis that there are either ideal levels and timing for cortisol exposure in the developing infant, or, at least, a range of acceptable levels. Exposure above or below that range, or during crucial time frames, may result in negative outcomes.

Aside from the effect on the stress-response-axis, cortisol increases during development in some studies show a decrease in synaptogenesis, hippocampal weight, and fewer glucocorticoid receptors in both the amygdala and the hippocampus. These changes are associated with poorer memory and decreased ability to learn, and all of these changes are found in conjunction with changes in gene expression within the placenta.

The Oxytocin system is another area that is being researched for its significance to human behavior. Oxytocin has been known as “the love hormone” but more accurately is responsible for setting appropriate social interactions in place — including the urge to nurture and protect young, mate and defend one’s mate, and socialize or compete with same-sex comrades in heterosexuals.

The oxytocin system is not only affected by the administration of exogenous oxytocin and oxytocin receptor antagonists but also by levels of steroid hormones including progesterone, testosterone, and estrogen. As with cortisol, these exposures during pregnancy and early postpartum result in hormonal imprinting that will guide future behaviors. These behavioral changes, or, rather, preset baselines for behaviors, result from changes in the fetal brain by way of gene expression, neuron function, cell morphology (shape and appearance of cells), and axonal guidance (process by which neurons send out axons to reach their targets).

Furthermore, a study on rats showed that a single dose of oxytocin at birth reduced the turnover of dopamine and serotonin in the brain of the rats at 4 months of age. These findings are significant considering that a number of conditions of the mind including autism and schizophrenia appear to be related to disturbances of the serotonin and dopamine systems.The hormonal imprinting of the oxytocin system during gestation appears to be responsible for many future outcomes, including anxiety levels, prosocial behaviors, addictive tendencies, parenting, pair-bonding and sexual behavior. When oxytocin receptor antagonists are administered we see changes in what we believe are oxytocin fueled behaviors. In some species we witness a decrease in aggression and competition for mates and an increase in anxiety. With application of oxytocin, we witness increases in mating behaviors, aggression, attentiveness to young, pair-bonding, and in some species (mice, prairie voles, and pigs), a decrease in same-sex socialization and an increase in competitiveness and in others the opposite.

The big question here is: What does the idea that hormonal fluctuations during gestation shape the genetic expression, behaviors, and actual brain structures of our offspring mean? First and foremost, it means that more research needs to be conducted to learn about hormonal imprinting and its effects on lifelong health before we even consider further tampering with the oxytocin systems in our offspring

through interventions like the induction of labor with oxytocin receptor antagonists, including Pitocin (exogenous oxytocin), as well as exercising caution when determining whether to introduce interventions that increase cortisol exposure.

At the same time, cortisol and oxytocin are only two of many hormones that a fetus is exposed to during gestation, and we would do well to further examine the effects of them all.

When considering the manner in which mental and behavioral health conditions are passed on from parent to offspring, hormonal imprinting must be looked at as a significant variable at play and researched as a possible means to prevent the inheritance of mental illness. If extreme hormonal fluctuations in the mother can be prevented and even levels of specific hormones manipulated to meet a range of ideal or normal exposure, it may be possible to stop the genetic predisposition to disadvantageous mental disorders that might be hard-wired during gestation.

In the meantime, it is safe to say that measures should be taken to decrease stress and improve familial and societal supports during childbearing to ensure the next generation has the fullest potential to thrive. Should we reach a point where we become able to gestate our progeny outside of a human body, using an artificial womb through ectogenesis, we must take great care in controlling for the timing, frequency, and level of exposure to hormones for developing and imprinting optimal health of body and mind.

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