THE INFLUENCE OF PREGNANCY ON THE GRAY MATTER OF THE MATERNAL BRAIN

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Annotation: This thesis explores the changes of the brain gray matter in pregnancy, highlighting classical and novel mechanisms of humoral modulation. Recent studies have demonstrated that pregnancy induces profound neurobiological adaptations, influencing both brain structure and function.

Keywords: Pregnancy, gray matter reduction, neural remodeling, behavior, cognition.

Pregnancy is a transformative period characterized by significant hormonal and physiological changes, yet its impact on the maternal brain remains an evolving field of research. These changes, including reductions in gray matter volume and modifications in cortical thickness, suggest an intricate process of neural remodeling that supports maternal behavior and cognition [1]. Generalized additive models revealed strong nonlinear relationships between weeks since conception and summary brain metrics. Total grey matter volume (GMV), summary cortical thickness (CT) and total brain volume linearly decreased during gestation and appeared to partially rebound postpartum. In contrast, global microstructural integrity of white matter increased throughout the first and second trimesters before returning to baseline levels in the postpartum period. Also were observed nonlinear patterns of lateral ventricle expansion and increased cerebrospinal fluid (CSF) rising in the second and third trimesters before dropping sharply postpartum. Consistent with the broader cortical reductions in GMV, several subcortical regions significantly reduced in volume across gestation. This included bilateral ventral diencephalon, caudate,

hippocampus and thalamus, along with left putamen and brain stem [2].

In assessing of the structural differences between the maternal and nulliparous brains by means of surface-based analyses, in line with the volumetric analyses, reduced cortical thickness across the postpartum period was find compared to the nulliparous group, with the greatest difference being at childbirth and then diminishing at the subsequent measurement time points.

In examining the surface characteristics across the postpartum period itself, was found an increase in cortical thickness from childbirth to 3 weeks postpartum in both hemispheres in the lateral and medial prefrontal cortices including the cingulate cortex, the parietal cortex, the posterior part of the temporal cortex and fusiform gyri, and the insular cortex. From 3 to 6 weeks postpartum, an increase in cortical thickness was found in the left middle frontal and inferior frontal gyri, and the right superior frontal gyrus and the superior parietal lobule. No increase was found from 6 to 9 weeks and 9 to 12 weeks postpartum. However, increased cortical thickness from 9 to 12 weeks was found in the right pre- and postcentral gyri extending to the supramarginal gyrus. Furthermore, contrasting the more distal time points, 12 weeks vs. 6 weeks postpartum, cortical thickness increase was observed in the right superior frontal, middle frontal and inferior frontal gyri as well as in the left middle and inferior temporal gyri.

Comparing the time points of childbirth and 12 weeks postpartum, a decrease in cortical thickness throughout the postpartum period was found in the left medial orbital gyrus and the right lingual gyrus. [3]

The dynamic neuroanatomic changes observed in gestational mothers were associated with fluctuations in two types of estrogens: estriol and estrone sulfate. Similarly, some early studies reported estradiol levels in the third trimester to be associated with GM volume changes before and after pregnancy in humans; both trajectories evolve together yet in opposite directions. The larger the increase and posterior decrease in estriol and estrone, the larger the decrease and posterior recovery in GM volume change. Estrogen surge during pregnancy is mainly due to placental production and consequently plummets after placental expulsion at

childbirth. In line with this, a turning point in estrogenic and cortical trajectories around childbirth was observed. This suggests that parturition is a critical phase in maternal brain remodeling that deserves more research attention. [4]

A positive association was detected between postpartum months and prefrontal cortical thickness. Moreover, higher cortical thickness within those prefrontal regions was associated with higher self-reported parental efficacy. [5]

There are researches that women who had pre-labor C-sections presented greater cortical increases from late pregnancy to early postpartum than those who initiated labor. During the first stage of labor, that is, dilatation, pro-inflammatory signals are released. Combined with the effects of estrogens, prostaglandins and oxytocin, they trigger uterine contractions, cervical dilation, cervical effacement and the rupture of fetal membranes. The extreme cascade of immune and endocrine adaptations of labor may also induce neuroplasticity. It is possible that mothers experiencing at least the first stage of labor may undergo further cortical reductions, reaching a lower cortical volume before reversing the trajectory. An alternative explanation could be that mothers who did not initiate labor have a faster neural recovery [6].

Although GMV differences within 1 week of childbirth were found to encompass all lobes of the brain, the classification performance between the maternal and nulliparous brains was overwhelmingly driven by the left amygdala, in addition to the left Heschl gyrus, the right pallidum, the right rectal gyrus and the cerebellum. The amygdala has been shown to express high densities of estradiol and progesterone receptors.

Estradiol stimulates the growth of dendritic spines. This enhances synaptic plasticity. It increases the level of neurotrophins (they include nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin-4 (NT-4)), which contribute to the survival of neurons and the formation of new synapses [7].

Estradiol decreases the percent of activated immature neurons in the dorsal dentate gyrus [8]. This hormone also lowers IL-4, IL-10, and IL-13 concentration

based on the age of first pregnancy and lowers Tumor Necrosis Factor alpha (TNFα), and CRP in dried blood spots (DBS) in the dorsal hippocampus regardless of parity [9].

Next property is concerned with enhancing of the activity of brain areas associated with emotions and social interaction (amygdala, anterior cingulate cortex). Increased estrogen levels links to an increase in working memory errors during cognitive tasks [10]. Sensitivity to emotional signals increases, which helps to respond better to the needs of the baby. Learning new forms of behavior related to motherhood is accelerated.

Oxytocin has similar properties, which enhances the plasticity of synapses in the areas of the brain responsible for attachment (hypothalamus, amygdala, anterior cingulate cortex); may affect neuronal complexity and long-term potentiation in hippocampal neurons; promotes the activity of mirror neurons involved in empathy and social communication; affects glial cells, helping to remodel neural connections. As result a strong emotional connection with the baby is formed. The sensitivity to social signals and facial expressions of the child increases.

Progesterone - modulates the activity of GABA receptors, which reduces the excitation of neurons and has a calming effect; regulates the development of new neural connections, especially in the hippocampus, the center of memory and learning. It decreases of cognitive flexibility (forgetfulness) as the brain focuses less on insignificant details.

The considerable shift of estradiol and progesterone during pregnancy is likely involved in the volumetric change in the amygdala during pregnancy and the postpartum period, with the medial and the dorsal amygdala networks, including the striatum, the anterior and posterior cingulate, the ventromedial prefrontal cortex and the insula being key elements in human maternal bonding. Less hostile behavior toward the child has been found to be predicted by the volumetric change of the bilateral amygdala, the temporal pole, the right olfactory gyrus, the left anterior cingulate, the bilateral thalamus and the cerebellum, regions involved in socio-emotional processing and social cognition.

Cortisol improves neuroplasticity in small amounts, but chronic stress (high levels of cortisol) can cause atrophy of neurons, especially in the hippocampus; it interacts with the dopamine system, changing motivation and behavioral reactions.

Consequences are: a moderate level of cortisol helps to concentrate on taking care of the child. Prolonged stress can cause a decrease in the volume of gray matter in the prefrontal cortex and hippocampus, which affects memory and emotion management.

Depression – a very common occurrence during gestational periods- is associated with increased cortisol levels. Chronic stress contributes significantly to depressive symptoms in other, even in non-pregnancy conditions and is linked to increased irritability, low mood, and constant worrying [10].

Prolactin – stimulates the growth of new neurons in the hippocampus, regulates the work of the dopamine system, affecting motivation and behavior. It promotes the remodeling of neural connections in areas responsible for parental behavior. Consequences are: increasing of maternal motivation and patience, enhancing neuroplasticity, helping to adapt to new responsibilities [3].

Conclusion: hormonal changes during pregnancy make the brain more flexible, improving its adaptation to motherhood. The postpartum changes in brain structures involved in social processes may have an incremental adaptive benefit in refining abilities to recognize and respond to infant needs, identify social and threatening stimuli, or promote mother-infant attachment.

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