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Postpartum Depression Changes Brain Structure in Mothers

Analysis by Dr. Joseph Mercola | January 09, 2025

STORY AT-A-GLANCE

- Women diagnosed with postpartum depression (PPD) exhibit distinct brain structure difference compared to women without it. Observations include larger gray matter volumes in regions like the putamen, pallidum, caudate and thalamus
- Estradiol polygenic risk scores influence brain volumes differently based on postpartum depression history, with a positive correlation in women with PPD and a negative correlation in those without
- Neurobiological changes during the peripartum period, driven by hormonal fluctuations, immune system adjustments and sleep disruptions, increase the risk of postpartum depression, affecting both mothers and their offspring
- Women with postpartum depression show increased cortical thickness in specific brain regions, such as the left superior frontal gyrus and right lingual gyrus, which correlates with depressive symptoms and challenges in mother-infant interactions
- Understanding brain structure differences and neurobiological changes will aid in developing targeted interventions for peripartum depression to help improve mental health outcomes for affected women

Postpartum depression (PPD) is a mood disorder affecting women during pregnancy or within the first year after giving birth. Characterized by persistent feelings of sadness, anxiety and fatigue, it significantly impacts a mother's ability to care for herself and her newborn child. It's drastically different from "baby blues," which typically resolve within a few weeks after giving birth.

The underlying causes of PPD are multifaceted. Hormonal changes during and after pregnancy play a significant role, as levels of estrogen and progesterone rise dramatically during pregnancy and drop sharply after childbirth. This hormonal rollercoaster will eventually affect mood and emotional stability.

Additionally, genetics make some women more susceptible to PPD. Environmental factors, such as stress, lack of sleep and the physical demands of caring for a newborn, also contribute to the development of this condition. These elements create a perfect storm that lead to PPD.

When these underlying causes converge, they disrupt the brain's normal functioning. Hormonal imbalances affect neurotransmitter systems, which are responsible for regulating mood and emotions. Now, researchers are attempting to understand how the human brain changes and adapts during this time in the hopes of helping new mothers manage their condition better.

The Brain Structure of Women with Peripartum Depression

Research published in Biological Psychiatry: Cognitive Neuroscience and Neuroimaging aimed to uncover the neurobiological distinctions between women who have experienced PPD and those who have not. The authors specifically focused on the basal ganglia, a group of structures in the brain associated with emotion, reward and decision-making processes, as well as the impact of estradiol polygenic risk scores (PRS) on brain morphology.[1]

The study involved 64 mothers diagnosed with major depressive disorder (MDD) — 30 had a history of PPD and 34 did not — who were recruited from a larger cohort of 219 patients in Milan. To compare brain structure between the two groups, the team utilized voxel-based morphometry analysis to study the gray matter volumes within specific regions of the basal ganglia.

The group with a history of PPD were found to have significantly larger gray matter volume in bilateral clusters that include the putamen, pallidum, caudate and thalamus

compared to those without PPD. This structural difference indicates that the basal ganglia plays a crucial role in the pathophysiology of PPD, and that it has a high concentration of estrogen receptors sensitive to hormonal changes.[2]

Furthermore, the research demonstrated that estradiol PRSs interact differently with brain volumes based on PPD history.[3] Specifically, in women with PPD, higher estradiol PRSs were associated with increased gray matter volumes in the basal ganglia clusters. In contrast, women without PPD showed a negative association between estradiol PRSs and gray matter volumes in these regions.[4]

The Impact of Estradiol on Brain Function

The study also explored how estradiol levels affect the basal ganglia's structure and function. For context, estradiol influences gene expression, dendritic spine density and neurotransmitter function within these brain regions.[5] These pathways contribute to the observed structural differences, indicating that hormonal fluctuations during the peripartum period trigger or exacerbate depressive symptoms in susceptible women.

Moreover, the basal ganglia's involvement in emotion regulation and decision-making provides a functional context for the structural differences observed. Altered basal ganglia structure and function have been linked to MDD in previously published studies, indicating that these regions play a role in the progression of depression.[6]

Overall, the study sheds new light on how hormonal and genetic factors interact to influence brain structure and function in the context of PPD. The identification of larger gray matter volumes in specific basal ganglia regions among women with PPD highlights the importance of considering both hormonal sensitivity and genetic predispositions in the diagnosis and treatment of this condition.[7]

More Neurobiological Changes Occur During the Peripartum Period

In a meta-analysis published in Social Cognitive and Affective Neuroscience, researchers explored the significant changes that occur in a woman's brain during pregnancy and after giving birth. In particular, they focused on understanding how hormonal shifts, immune system adjustments, sleep disturbances and increased stress levels impact women's mental health and brain structure.[8]

After comparing pregnant and postpartum women to women who were not pregnant, findings show that more than a quarter of women experience depressive symptoms during this period. Also, symptoms are linked to notable changes in the brain's structure and function. These are driven by fluctuations in hormones and the immune system, as well as disruptions in sleep and increased caregiving responsibilities after giving birth.[9]

Researchers discovered that during the peripartum period (the period shortly before, during and right after giving birth[10]), women undergo substantial structural changes in their brains. Specifically, there is a reduction in gray matter volume, particularly in the hippocampus, a region crucial for memory and learning.

Additionally, the amygdala, which is involved in processing emotions, is altered. These changes are not just temporary, but extend beyond the immediate postpartum period.[11]

Hormonal fluctuations play a critical role in these brain changes. The drop in estrogen and progesterone levels after childbirth triggers a cascade of chemical reactions in the brain, leading to mood swings and increased vulnerability to depression. These hormones are essential for maintaining pregnancy, and their rapid decrease subsequently affects various brain regions responsible for emotional regulation and cognitive functions.[12]

The immune system also significantly adjusts during pregnancy to protect both the mother and the developing fetus. This balance impacts the brain by altering immune cell function, which influence neurodevelopmental processes. Disruptions in immune function contribute to structural brain changes and increase the risk of developing depressive symptoms.[13]

Sleep disruption is another major factor contributing to neurobiological changes. Many new mothers experience poor sleep quality or insufficient sleeping time, which affects the amygdala, making it more reactive and heightening emotional responses. This increased reactivity leads to higher emotional intensity and volatility, further exacerbating symptoms of depression and anxiety.[14]

Psychosocial stress, stemming from the challenges of caregiving and adjusting to motherhood, also impacts brain structure. Chronic stress leads to alterations in brain regions involved in reward processing and decision-making, such as the striatum and prefrontal cortex. These changes impair cognitive functions like memory and information processing, making it harder for new mothers to cope with daily responsibilities.[15]

Structural Brain Abnormalities Found in Postpartum Depression

In another study, published in Behavioural Brain Research, a team investigated the differences in brain structures between women experiencing PPD and those without it. The research focused on examining both the cortical and subcortical areas of the brain, involving 29 women diagnosed with PPD and 23 healthy postpartum women as a control group. All participants were right-handed, aged between 20 and 40, and were one to two months postpartum.[16]

The study revealed that women with PPD exhibited increased thickness in several specific regions of the brain. Specifically, there was a significant increase in the cortical thickness of the left superior frontal gyrus, cuneus, right lingual gyrus and fusiform gyrus compared to the healthy postpartum women group.[17] Additionally, these women showed regional inflation in the right pallidum, a subcortical structure involved in emotion regulation and reward-processing.

Going deeper into the findings, the study found that the depression scores were significantly higher in the PPD group than in the healthy group, indicating more severe depressive symptoms.[18] Interestingly, there was no significant difference in local

gyrification index — another tool to measure cortical morphology — between the two groups, suggesting that certain aspects of brain folding were not impacted by PPD.[19]

The increased cortical thickness in the affected regions highlights significant alterations in areas responsible for cognitive control, emotional regulation, and visual processing. For example, the left superior frontal gyrus is key for executive functions, including decision-making and managing emotions.

Meanwhile, the cuneus and fusiform gyrus are integral to processing visual information and recognizing facial emotions, which are essential for social interactions and bonding with the infant.[20]

Moreover, the study highlighted that the regional inflation in the right pallidum is linked to the limbic-cortical-striatal-pallidal-thalamic (LCSPT) circuit. This circuit plays a crucial role in regulating emotions and processing rewards. Dysfunction in the pallidum leads to symptoms such as lack of motivation, inability to feel pleasure and persistent negative thoughts — all of which are common in PPD.

Essentially, the enlargement of the pallidum observed in women with PPD is linked to difficulties in responding positively to infant stimuli, which will adversely affect maternal behaviors.[21]

Four Ways to Help Mothers Manage Postpartum Depression

Dramatic hormonal shifts, as well as compounding stress during pregnancy and post-birth will inevitably create significant changes in a mother's brain structure and function. Understanding and preparing for these changes will help support their mental health during this crucial time. To manage the symptoms, here are practical strategies I recommend:

1. **Prioritize sleep and recovery —** Sleep deprivation significantly impacts brain regions involved in emotional regulation, as well as overall cognitive function. Make sleep a priority by coordinating with family members to ensure you get seven to eight hours of rest while they help take care of the baby. For tips on how to improve

your sleep quality, read "How Sleep Deprivation Impairs Cognitive Performance and Learning."

2. **Engage in regular, moderate-intensity exercise —** Once you're able, I encourage you to go for regular walks outdoors. As you start moving again, your body gains a dose-dependent decrease in depression, sarcopenia and overall mortality. Exercising with a friend or a group class is even better, as it adds a social support component compared to exercising alone.

3. **Support your nutrition with brain-boosting foods —** Decrease your intake of inflammatory foods like processed sugar and vegetable oils, which affect brain function. Focus on foods rich in the vitamin B family, as this nutrient group is crucial for brain health and emotional regulation.

4. **Optimize your hormone balance —** Focus on supporting progesterone production to counteract the rapid drop in hormones after childbirth. Getting adequate sun exposure supports vitamin D production, which works synergistically with progesterone for optimal brain function. For proper administration of progesterone, read my detailed instructions below.

How to Use Progesterone

Before you consider using progesterone, it is important to understand that it is not a magic bullet, and that you get the most benefit by implementing a Bioenergetic diet approach that allows you to effectively burn glucose as your primary fuel without backing up electrons in your mitochondria that reduces your energy production. My new book, "Your Guide to Cellular Health: Unlocking the Science of Longevity and Joy," covers this process in great detail.

Once you have dialed in your diet, an effective strategy that can help counteract estrogen excess is to take transmucosal progesterone (i.e., applied to your gums, not oral or transdermal), which is a natural estrogen antagonist. Progesterone is one of only

four hormones I believe many adults can benefit from. (The other three are thyroid hormone T3, DHEA and pregnenolone.)

I do not recommend transdermal progesterone, as your skin expresses high levels of 5-alpha reductase enzyme, which causes a significant portion of the progesterone you're taking to be irreversibly converted primarily into allopregnanolone and cannot be converted back into progesterone.

Ideal Way to Administer Progesterone

Please note that when progesterone is used transmucosally on your gums as I advise, the FDA believes that somehow converts it into a drug and prohibits any company from advising that on its label. This is why companies like Health Natura promotes their progesterone products as "topical."

However, please understand that it is perfectly legal for any physician to recommend an off-label indication for a drug to their patient. In this case, progesterone is a natural hormone and not a drug and is very safe even in high doses. This is unlike synthetic progesterone called progestins that are used by drug companies, but frequently, and incorrectly, referred.

Dr. Ray Peat has done the seminal work in progesterone and probably was the world's greatest expert on progesterone. He wrote his Ph.D. on estrogen in 1982 and spent most of his professional career documenting the need to counteract the dangers of excess estrogen with low LA diets and transmucosal progesterone supplementation.

He determined that most solvents do not dissolve progesterone well and discovered that vitamin E is the best solvent to optimally provide progesterone in your tissue. Vitamin E also protects you against damage from LA. You just need to be very careful about which vitamin E you use as most supplemental vitamin E on the market is worse than worthless and will cause you harm not benefit.

It is imperative to avoid using any synthetic vitamin E (alpha tocopherol acetate — the acetate indicates that it's synthetic). Natural vitamin E will be labeled "d alpha

tocopherol." This is the pure D isomer, which is what your body can use.

There are also other vitamin E isomers, and you want the complete spectrum of tocopherols and tocotrienols, specifically the beta, gamma, and delta types, in the effective D isomer. As an example of an ideal vitamin E, you can look at the label on our vitamin E in our store. You can use any brand that has a similar label.

You can purchase pharmaceutical grade bioidentical progesterone as Progesterone Powder, Bioidentical Micronized Powder, 10 grams for about $40 on many online stores like Amazon. That is nearly a year's supply, depending on the dose you choose.

However, you will need to purchase some small stainless steel measuring spoons as you will need a 1/64 tsp, which is 25 mg and a 1/32 tsp, which is 50 mg. A normal dose is typically 25-50 mg and is taken 30 minutes before bed, as it has an anti-cortisol function and will increase GABA levels for a good night's sleep.

Unfortunately, this vendor frequently runs out of product, and if that's the case, then you can use **Simply Progesterone by Health Natura**. It's premixed with vitamin E and MCT oil. Again, while Health Natura states that its product is for "topical use only," I recommend applying it transmucosally, by rubbing it on your gums.

If you are a menstruating woman, you should take the progesterone during the luteal phase or the last half of your cycle, which can be determined by starting 10 days after the first day of your period and stopping the progesterone when your period starts.

If you are a male or non-menstruating woman, you can take the progesterone every day for four to six months and then cycle off for one week. The best time of day to take progesterone is 30 minutes before bed as it has an anti-cortisol function and will increase GABA levels for a good night's sleep.

This is what I have been personally doing for over a year with very good results. I am a physician so do not have any problems doing this. If you aren't a physician, you should consult one before using this therapy, as transmucosal progesterone therapy requires a doctor's prescription.

Sources and References

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