The Synapse: Intercollegiate science magazine

Volume 34 | Issue 1 Article 8

11-1-2022

The Hidden Sadness of Pregnancy: Postpartum Depression and the Effects of Preventative Medicine

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The Hidden Sadness of Pregnancy

Postpartum Depression and the Effects of Preventative Medicine

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It is expected in today's world that a new parent would feel joy and a sense of accomplishment after nine long months of pregnancy. Some feel the obsession and overwhelming need to look after their child's every move. It is normal for parents to also feel tiredness, anxiety, and experience general difficulties after bringing new life into the world. However, one must take into consideration the sadness that gets overlooked far too often. For some, this sadness can persist months after the child is born.

Postpartum depression (PPD) affects approximately 10 - 18 percent of pregnancy capable people. It manifests very similarly to the more general major depressive disorder; sadness, indifference, anxiety, changes in energy, in sleep, in appetite, and thoughts of guilt or suicide are all hallmark symptoms.

What differentiates PPD from major depressive disorder is the timing of the onset of symptoms. Additionally, the new child often plays a significant part in the symptoms of PPD. For instance, new parents with PPD may find it difficult to properly bond with and care for the new child. The new parent might feel especially anxious or even have thoughts of harming the child. Consequently, in some extreme cases the child of a parent with PPD is at risk for suffering from low self-esteem, low intellectual skills, child abuse, and even infanticide, mainly if the PPD goes untreated.

Effective treatments for PPD do exist; however, the earlier they are implemented, the more effective they are at reducing symptoms and harm to both parent and child. Therefore, predicting which pregnancy capable individuals are likely to develop PPD and treating them before or as symptoms manifest would go a long way towards improving health outcomes for both parent and child. A set of newly discovered epigenetic biomarkers may pave the way for this type of preventative treatment.

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Understanding the pathophysiology of PPD is vital to appreciate the effect the biomarkers have. The serotonergic system, the network neurons thought to regulate mood primarily through serotonin, is likely involved in producing the symptoms of PPD. Estrogen, a hormone whose presence steadily increases during pregnancy before plummeting after childbirth, is known to interact with the serotonergic system. In animal models of depression, estrogen's effects are similar to those of serotonergic antidepressants. While one might conclude from this that the drop in estrogen after childbirth causes PPD, the reality is not quite so simple. A reduction in estrogen alone does not predict PPD. Instead, researchers theorize that parents who develop PPD have an increased sensitivity to the effects of rapidly declining estrogen in the body.

A major function of estrogen in the body is the promotion of the transcription of specific genes. Interestingly, estrogen seems to induce epigenetic modifications in these genes as well. These epigenetic modifications are changes or additions to the structure of DNA that modify gene expression rather than the genetic code itself. One type of epigenetic modification is known as methylation, wherein a methyl group is attached to a cytosine. Estrogen is known to modify the pattern of methylation in genes it acts on. While the specific effects estrogen has on particular genes are not well understood, they are also not relevant for testing for risk for PPD. As mentioned above, it is theorized that what separates child-bearing people who develop PPD from child-bearning people who do not is the body's increased sensitivity to estrogen and its subsequent effects. This increased sensitivity may manifest as a difference in methylation patterns between at-risk and non-at-risk populations.

The first step to finding these differentially methylated regions (DMRs) is to get a sense of which genes are methylated by exposure to estrogen. One research group used a mouse model and specifically examined the DNA of hippocampal neurons after exposure to estrogen. The hippocampus was specifically chosen because it is believed that estrogen's primary effect on mood is mediated there. After applying estrogen and analyzing the DNA of hippocampal neurons, over 1,000 DMRs were found. With this data, the researchers turned to human application.

First, each differentially methylated locus was "translated" from the mouse genome by finding its analogous location in the human genome. The data was then pruned so that only the loci likely to be significantly related to PPD were further examined. These loci were then used individually to create a statistical model predicting whether or not a child-bearing person would develop PPD.

A group of people whose PPD status was already known had their methylation levels at each locus recorded. This data was used to train a model from each locus, whose accuracy was determined by applying it to a separate group of people whose PPD status was also already known. To construct the most robust model possible, each single-locus model had another locus "added" to it. These combination models would only be kept if the accuracy was increased. At the end of this process, a model was developed with an accuracy of ~90 percent using two loci: the promoter region of the gene HP1BP3 and the promoter region of the gene TTC9B.

This statistical model was then replicated and tested on new groups of subjects, generally performing with an accuracy of ~80 percent for both child-bearing people with and without a history of mood disorders prior to pregnancy. While the results of this experiment are promising, it is important to look forward to the next step of this research: discovering the underlying mechanisms that enable this model to work. Though it is known that both genes have ties to estrogen signaling, HP1BP3 associating with

an estrogen receptor and TTC9B expression being responsive to gonadal hormones such as estrogen, their more specific functions still need to be fully understood. Establishing these functions might bridge the gap between prediction with timely treatment and true prevention.

However, we now have biomarkers that predict PPD and are detectable in blood once pregnancy has begun but, crucially, before childbirth. Suppose a doctor believes a child-bearing person to be at risk for PPD, in that case, intervention with antidepressant medication could be initiated during or shortly after pregnancy to effectively and proactively treat the symptoms. This would go a long way towards improving both the parent and child's health outcomes.

Throughout the course of a person's pregnancy, they will go through a dizzying number of procedures, tests, and diagnostics to ensure their health and the health of the soon-to-be baby. If one of the tests has a positive result, and the doctor believes they are at high-risk for PPD, the parent could become anxious and scared. Luckily, due progress in OB/GYN medicine, treatments are available and PPD can be treated preventatively. As soon as the pregnancy is completed, the parent can begin taking antidepressants. While there were a few signs of PPD to begin with, taking preventative action will reduce the symptoms and the parent can begin this chapter of life with their new baby.