Quantum biology has identified the fact that some medications used for hypertension (e.g. calcium channel blockers) can also function as serotonin reuptake inhibitors.

If a woman's serotonin levels are adequate but her levels of aldosterone are high the use of calcium channel blockers could be prescribed to address the hypertension but inadvertently create serotonin toxicity.

One of the results of using inappropriate medications can be imbalances in the neuropeptides NPY for catecholamines and pancreatic polypeptide for brain derived neurotrophic factors that include serotonin for emotions.

Verification by qualified computation biologists in necessary but one of the consequences of excessive serotonin can be drug induced Parkinson's disease.

https://neurosciencenews.com/antidepressants-pregnancy-15427/

Are some antidepressants less risky for pregnant women?

NEUROSCIENCE NEWSJANUARY 8, 2020

Summary: *Alteration of placental serotonin levels due to maternal depression or antidepressant use may be associated with the disruption of placental estrogen production.*

Source: *INRS*

About one in ten women in Québec will suffer from depression during pregnancy. Without treatment, the illness carries risks for both mother and child. Yet antidepressants are not without consequences for fetal development. The team of professor Cathy Vaillancourt at the Institut National de la Recherche Scientifique (INRS) is studying the effects of these drugs in order to identify the least harmful ones.

Professor Vaillancourt, in collaboration with the teams of Professors J. Thomas Sanderson and Nicolas Doucet of the INRS, has just modeled for the first time the interaction of commonly used antidepressants with estrogen, and more specifically with the enzyme that synthesizes the estrogen: aromatase. It is an important contribution since estrogen production is essential to the development of the fetus and to the mother's physiological adaptation during pregnancy. The results of their study were recently published in The *Journal of Steroid Biochemistry and Molecular Biology*.

Prescribing antidepressants for pregnant women is controversial. Studies show that, when administered to mothers during pregnancy, some of these treatments are associated with a risk of heart and lung malformations in newborns. Others are thought to result in impaired cognitive development, including autism, in children.

Estrogen as a target for antidepressants

The harmful effects of antidepressants are thought to be due to their interaction with certain key hormones. Most antidepressants prescribed to pregnant women target serotonin, a hormone produced both in the brain and, as shown by Professor Vaillancourt's team in 2017, in the placenta. This is the family of antidepressants called selective serotonin reuptake inhibitors (SSRIs) such as Zoloft, Celexa or Prozac. However, estrogen would also be targeted by these treatments.

"We wanted to see how the antidepressants that have been developed to block the serotonin transporter also affect aromatase. Using molecular models, we found that all the antidepressants we analyzed seemed to be able to bind directly to the enzyme and regulate its activity. This remains to be confirmed and the precise mechanism needs to be further investigated," reports Cathy Vaillancourt, lead author of the study.

Her doctoral student tested the effect of different types of antidepressants on placenta samples collected after delivery. "The antidepressants we chose to test are those most commonly prescribed in pregnant women, namely sertraline (Zoloft), venlafaxine (Effexor), fluoxetine (Prozac), paroxetine (Paxil), and citalopram (Celexa)," says Andrée-Anne Hudon Thibeault "By comparing different doses and molecules, we were able to uncover some of their specificities."

By observing the effects of antidepressants on the placenta's hormonal system, the team can determine in advance if there will be a risk for the fetus. "Fetal development is strongly linked to the placenta. Every healthy fetus has a healthy placenta," maintains Vaillancourt.

Safer antidepressants

Not all types of antidepressants have these harmful effects. Not all pharmacological molecules have the same hormonal affinity. "Depending on its form, a molecule may not interact the same way with estrogen and may therefore be less harmful to the developing fetus," asserts Professor Vaillancourt, who specializes in the involvement of maternal exposure to environmental and drugs factors in the endocrinology of the human placenta.

It's more a matter of the pharmacological molecule being administered and the dosage. "By testing several types of antidepressants at varying doses, our work will contribute to better choices regarding the type of antidepressant and the dose prescribed for pregnant women, while minimizing the side effects on the course of pregnancy and on fetal development," says Andrée-Anne Hudon Thibeault, primary author and recent PhD graduate of INRS.

Discontinuing medication isn't always advisable. Depression can have serious consequences if left untreated. "Depression is one of the leading risk factors for suicide in pregnant women," says Vaillancourt. "Some studies suggest that depression can also compromise fetal development, due in part to poor lifestyle habits."

At the same time, Professor Vaillancourt is collaborating with a team of researchers in Vancouver who are studying a cohort of pregnant women and following their children over the long term. "This will give us a nice map of the various effects in women and the consequences for children's heart and brain development," says Vaillancourt. "We're still in the early stages of the project, but I'm confident that some antidepressants are safer and others can be developed for use during pregnancy."

Funding: This research was supported by funding from March of Dimes and the Natural Sciences and Engineering Research Council of Canada (NSERC).

ABOUT THIS NEUROSCIENCE RESEARCH ARTICLE

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"Serotonin and serotonin reuptake inhibitors alter placental aromatase". Andrée-Anne Hudon Thibeault, Yossef López de los Santos, Nicolas Doucet, J. Thomas Sanderson et Cathy Vaillancourt.
*Journal of Steroid Biochemistry and Molecular Biolog*doi:10.1016/j.jsbmb.2019.105470.

Abstract

Serotonin and serotonin reuptake inhibitors alter placental aromatase

Serotonin reuptake inhibitors (SRIs) are currently the main molecules prescribed to pregnant women that suffer from depression. Placental cells are exposed to SRIs via maternal blood, and we have previously shown that SRIs alter feto-placental steroidogenesis in an in vitro co-culture model. More specifically, serotonin (5-HT) regulates the estrogen biosynthetic enzyme aromatase (cytochrome P450 19; CYP19), which is disrupted by fluoxetine and its active metabolite norfluoxetine in BeWo choriocarcinoma cells. Based on molecular simulations, the

present study illustrates that the SRIs fluoxetine, norfluoxetine, paroxetine, sertraline, citalopram and venlafaxine exhibit binding affinity for the active-site pocket of CYP19, suggesting potential competitive inhibition. Using BeWo cells and primary villous trophoblast cells isolated from normal term placentas, we compared the effects of the SRIs on CYP19 activity. We observed that paroxetine and sertraline induce aromatase activity in BeWo cells, while venlafaxine, fluoxetine, paroxetine and sertraline decrease aromatase activity in primary villous trophoblast. The effects of paroxetine and sertraline in primary villous trophoblasts were observed at the lower doses tested. We also showed that 5-HT and the 5-HT2A receptor agonist 2,5-dimethoxy-4-iodoamphetamine (DOI) induced CYP19 activity. An increase in phosphorylation of serine and tyrosine and a decrease in threonine phosphorylation of CYP19 was also associated with DOI treatment. Our results contribute to better understanding how 5-HT and SRIs interact with CYP19 and may affect estrogen production. Moreover, this study suggests that alteration of placental 5-HT levels due to depression and/or SRI treatment during pregnancy may be associated with disruption of placental estrogen production.