The contraceptive pill also affects the brain and the regulation of emotions, say researchers

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Oral contraceptives, also known as birth control pills, are used by more

than 150 million women worldwide. Approximately one-third of teenagers in North America and Europe use them, making them the most prescribed drug for teenagers.

It is well known that oral contraceptives have the power to alter a woman's menstrual cycle. What's less well known is that they can also have an effect on the brain, particularly in the regions that are important for regulating emotions.

As a doctoral student and professor of psychology at UQAM, we were interested in the impact of oral contraceptives on the brain regions involved in emotional processes. We published our results in the journal *Frontiers in Endocrinology*.

How does the pill work?

There are several methods of hormonal contraception, but the most common type in North America is the contraceptive pill, more specifically, combined oral contraceptives (COCs). These are made up of two artificial hormones that simulate one of the types of estrogen (generally ethinyl estradiol) and progesterone.

Like natural hormones, known as endogenous hormones, the artificial hormones contained in the pill, known as exogenous hormones, have an effect on the brain. They bind to receptors in different areas and signal the brain to reduce the production of endogenous sex hormones. It is this phenomenon that leads to the cessation of menstrual cycles, preventing ovulation.

In other words, while using COCs, users' bodies and brains are not exposed to the fluctuations in sex hormones typically seen in women with a natural cycle.

The pill's effects on the brain: Neuroscience to the rescue!

When they start taking COCs, teenage girls and women are informed of their different side effects, mainly physical (nausea, headaches, weight changes, breast tenderness). However, the fact that sex hormones affect the brain, particularly in areas important for regulating emotions, is not generally discussed.

Studies have associated the use of COCs with poorer ability to regulate emotions and a higher risk of developing psychopathologies.

In addition, women are more likely than men to suffer from anxiety and chronic stress disorders. Given the widespread use of COCs, it is important to gain a better understanding of their effects on the anatomy of the brain regions that are responsible for emotional regulation.

We therefore conducted a study to examine the effects of COCs on the anatomy of brain regions involved in emotional processes. We were interested in the effects associated with their current use, but also in the possibility of lasting effects, i.e. whether COCs could affect brain anatomy even after women stopped taking them.

To do this, we recruited four profiles of healthy individuals: women currently using COCs, women who had used COCs in the past, women who had never used any method of hormonal contraception, and men.

Using brain imaging, we found that only women currently using COCs had a slightly thinner ventromedial prefrontal cortex than men. This part of the brain is known to be essential for regulating emotions such as fear. The scientific literature shows that the thicker this region is, the better the emotional regulation will be.

COCs could therefore alter emotional regulation in women. Although we have not directly tested the link between brain morphology and mental health, our team is currently investigating other aspects of the brain and mental health, which will allow us to better understand our anatomical findings.

An effect associated with the dose, but that doesn't last

We tried to better understand what could explain the effect using COCs on this region of the brain. We discovered that it was associated with the dose of ethinyl estradiol. In fact, among COC users, only those using a low-dose COC (10–25 micrograms)—not a higher dose (30–35 micrograms)—were associated with a thinner ventromedial prefrontal cortex.

It may seem surprising that a lower dose was associated with a cerebral effect…

Given that all COCs reduce concentrations of endogenous sex hormones, we propose that estrogen receptors in this brain region may be insufficiently activated when low levels of endogenous estrogen are combined with a low intake of exogenous estrogen (ethinyl estradiol).

Conversely, higher doses of ethinyl estradiol could help to achieve adequate binding to estrogen receptors in the prefrontal cortex, simulating moderate to high activity similar to that of women with a natural menstrual cycle.

It is important to note that this lower gray matter thickness was specific to current COC use: women who had used COCs in the past showed no thinning compared to men. Our study therefore supports the reversibility

of the impact of COCs on cerebral anatomy, in particular on the thickness of the ventromedial prefrontal cortex.

In other words, the use of COCs could affect brain anatomy, but in a reversible way.

And now?

Although our research has no direct clinical orientation, it is helping to advance our understanding of the anatomical effects associated with the use of COCs.

We are not calling for women to stop using their COCs: adopting such discourse would be both too hasty and alarming.

It's also important to remember that the effects reported in our study appear to be reversible.

Our aim is to promote basic and clinical research, but also to increase scientific interest in women's health, an area that is still understudied.

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