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Could the Contraceptive Pill Pose a Risk to Brain Development in Young Girls?

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Abstract

It is well-established that adolescence, for both girls and young men, is a period of anatomical and functional transformation of the brain, enabling them to acquire the aptitudes of adults, that is, for girls, the aptitudes of adult women and mothers. According to several scientific studies, the hormones secreted by the ovaries, estrogen and progesterone contribute to this brain development during adolescence. Therefore, there is concern that hormonal contraceptives may modify the temperament of adolescent girls by altering their hormonal balance. In this article, we presented research showing that: (1) brain changes during adolescence occur in parallel with changes in sex hormone levels; (2) the gradual establishment of natural cycles during adolescence creates an estrogenic environment that is very different from that produced by hormonal contraceptives; and (3) hormonal contraceptives can cause changes in temperament and, consequently, personality. These facts are little-known in the medical community. It is therefore necessary to disseminate this information within the medical profession. It is also essential to provide young girls and their parents with comprehensive information before prescribing hormonal contraceptive treatment. This will enable them to make informed decisions.

Nontechnical summary: Adolescence is a period of brain transformation that prepares girls for their lives as women and perhaps mothers. The hormones of the menstrual cycle contribute to this brain change. The level of these hormones comes from the gradual establishment of the female cycle. The evolution and nature of these hormones are very different from those produced by hormonal contraception. We conclude that it is necessary to inform young girls and their parents about these effects before prescribing hormonal contraception.

Short Summary: Scientific evidence suggests that contraceptive hormones may pose a risk to brain development in young girls.

Keywords

adolescence, hormonal contraception, brain, behavior, menstrual cycle

Introduction

Hormonal contraceptives are now widely prescribed to young girls. In many cases, parents have willingly recommended it to their daughters to protect them from unwanted pregnancy, to reduce the pain of menstruation, or to treat a skin condition such as acne or hyperpilosity.

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However, there have been calls to question this practice: (1) Educators have warned of the possible negative effects of this prescription on the personal and relational lives of young people; (2) the fear of the consequences of a change in the sexual relationship, originally a celebration of love and the source of the transmission of life, has been expressed; (3) psychological disorders, altered moods, and an increased risk of depression after the start of use have been reported in the scientific press (Masama et al. 2022); (4) in addition, cases of phlebitis, embolism, and strokes have made the headlines (Correia et al. 2021; Saddik et al. 2022) and have been followed by widespread criticism of hormonal contraceptives on social networks; (5) finally, scientists have pointed out that if contraceptives are prescribed for medical reasons, such as correcting skin disorders, the pros and cons should be weighed: the negative effects must not outweigh the positive effects (Plu-Bureau and Raccah-Tebeka 2022).

If we are discussing the benefits of prescribing oral contraceptives to adolescents, each of these aspects deserves attention. With a focus on the contribution of neuroscience, our discussion will be limited to the potential impact of hormonal contraceptives on brain development in young girls during adolescence and beyond. This is a major concern.

A number of striking neuroscientific findings point to a direct effect of hormonal contraceptives on the brain. We have the following for example:

- Hormonal contraception has an impact on women's verbal and spatial abilities (Griksiene and Ruksenas 2011).
- Women using hormonal contraceptives have a thicker prefrontal cortex than women not using contraceptives (Pletzer et al. 2010).
- Hormonal contraceptive users are similar to other women in their performance but show male-type brain activation (Pletzer et al. 2014).

It is well-established that adolescence, for both girls and young men, is a period of anatomical and functional transformation of the brain (Sturman and Moghaddam 2011; Siegel 2014), enabling them to acquire the aptitudes of adults, that is, for girls, the aptitudes of adult women and mothers; the ability to make the transition from the life of the family in which they were born to social life; and finally, the ability to discern. According to several scientific studies, the hormones secreted by the ovaries, estrogen, and progesterone contribute to this brain development (Sisk and Zehr 2005; Op de Macks et al. 2016) during adolescence. It is therefore feared that hormonal contraceptives, by altering the hormonal balance, can have adverse effects on the brain development of adolescent girls.

First, we will provide a brief overview of the role of temperament in personality development. Then, we will review current knowledge on the following four subjects:

1. Adolescence is a period of personality structuring.
2. The hormones of the menstrual cycle are involved in the development of the female brain.
3. The gradual onset of the female cycle gives young girls their hormonal profile, which differs considerably from that established by hormonal contraception.
4. What does science tell us about the effects of hormonal contraceptives on the brain?

In conclusion, we will draw some recommendations from this review.

From Temperament to Personality

Innate inclinations and aptitudes constitute what is known as a person's temperament: a set of innate psychological and physiological traits. These traits form the basis for the subsequent development of personality, which is defined as what makes a person distinct from everyone else, both psychologically and intellectually.

Scientists often use the term "motivation" to refer to inclinations. This is the natural, inner force that directs a person spontaneously or voluntarily towards an object, taste, or goal. It is important to use discernment when deciding whether to act on one's inclinations. The tendency to analyze a situation rather than guess what is happening (intuition), which is more common in men than in women, is an example of a gender-specific inclination (Baron-Cohen 2009).

Aptitudes are the qualities that enable certain performances. Aptitudes are innate and develop through practice. One example of a difference in aptitude between men and women is that men often find it easier to remember the bigger picture than the details, unlike women (Cahill et al. 2004).

The role of temperament in personality development is neither constant nor instinctive. For instance, testosterone, the primary sex hormone in men, can have different effects depending on the context. In a macho environment, it can incite violence. Conversely, in a context that promotes peace and sharing, testosterone encourages greater generosity (Dreher et al. 2016).

Just as muscles develop through physical exercise, the brain develops based on each individual's experiences, education, and actions. Neural plasticity, or the brain's ability to create, break down, or reorganize neural networks and connections between neurons, is at the heart of this development.

Thus, although they share a common humanity, men and women are born with different inclinations and aptitudes. These innate gifts develop to varying degrees depending on an individual's culture, education, and free choices. Adolescence is a crucial time of hormonal-dependent brain development.

Adolescence is a Period of Personality Structuring

Adolescence begins with puberty and continues until adulthood: it lasts twelve years (Siegel 2014). It's not a silly age, it's a molt of the brain, as the sciences indicate: the profound nature of adolescence is a "rewiring of a brain." Just as the body of an adult man or woman is radically different from that of a child, the brain of an adult is very different from that of a child because, during adolescence, the brain is radically transformed (Lerner and Steinberg 2009).

Adolescence is a time of three acquisitions: (1) the ability to transmit life, both physically and psychologically; (2) openness to social life; and (3) discernment.

Puberty is mainly about passing on life. The next stage of adolescence is participating in social life. Emerging adulthood is about discernment.

Ability to Transmit Life, Physically and Mentally

The foundations of the female or male temperament are laid in the womb and in the first year after birth (minipuberty) by the XX or XY chromosome pairs and hormones secreted by the fetus and then the newborn (Arnold, Rissman and Vries 2003).

The temperament, like the rest of the body, resumes its development at puberty under the effect of hormones secreted by the ovaries in girls and the testicles in boys. Each then acquires the skills needed to pass on life: girls and boys become fertile and attractive to each other. The girl's body becomes capable of carrying and nourishing a child. These skills are both psychological (aptitudes and inclinations useful for conjugal life and motherhood) and bodily (sexuality, fertility, breastfeeding). The evolution of the brain aims not only to make the young woman fit for sexuality and fertility but also to make the young man fit for fatherhood.

However, by the end of puberty, around the age of fourteen to sixteen, girls and boys have not yet acquired the other skills of adulthood, which continue to develop until after the age of twenty.

Opening Up to Social Life

The four years following the end of puberty are a phase of further development of the ability to

live in society. Note that these three four-year periods should not be considered strictly. Each period may start earlier or later and may be shorter or longer. The suggested durations are approximate.

This transition from life within the family to life in society is observed in humans as in other mammals (Adriani et al. 2004). It is not simply a cultural effect; it has a genetic basis. The way in which young people are raised during these years helps to equip them with the skills they need to support themselves and any family they may have. This is a time when young people develop strategies for being accepted by their peers. Boys learn what it means to be a man and a father in society and discover how they are perceived by girls and women. Girls also see what it means to be a woman and a mother in society and discover how they are perceived by boys and men. It's a time of doubt and hope: "Later, I'll do like that…."

Learning to Discern

The last four years of adolescence, around the age of twenty, are a period of strong development of the ability to discern, that is, to make a decision taking into account both the practical and emotional dimensions of the situation. This is a remarkable feature of the human species. A neuroscience specialist, Robert Sapolsky (2017), states that around the age of twenty, thanks in particular to the strong development of the prefrontal lobe, young people develop the ability to "do even the most difficult thing, if it's the right thing to do!" They become more capable of commitment because they have acquired more freedom. In fact, they are less dependent on their emotions than in the preceding teenage years, due to the development of the prefrontal lobe of their brain, which plays a key role in rational analysis. Exchanges between the prefrontal lobe and the cerebral amygdala, where emotions are managed, are key to the discernment process.

Finally, specialists in adolescence point out the importance of education and the actions of young people in the development of the brain (Siegel 2014). What is experienced at this age will have long-term repercussions. This confirms the importance of this period for everyone's future.

The Hormones of the Menstrual Cycle Play a Part in the Development of the Female and Maternal Psychology

Adolescent Hormones Play a Role in the Development of a Girl's Temperament

Sex hormones (testosterone in men, estrogen and progesterone in women) have two types of effect on the brain: an *activating* effect, which gives a particular dynamism when the hormones are in greater quantity (the effect ceases when secretion of the hormone stops), and an *organizing* effect, which organizes the brain at specific periods in life (the effect of the hormone continues after secretion stops).

Adolescence is a period marked by two major changes:

- The onset of hormonal secretions (mainly testosterone in men, estrogen and progesterone in women).
- The start of a second period during which hormones have an *organizing* effect (the first period running from in utero life to the end of the first year after birth). This period lasts throughout adolescence.

As hormone secretions are sex-specific, they will induce a specific brain development, specific to women or specific to men (Vigil et al. 2016). Thus, a young girl's natural hormones play an important part in the development of her brain (Perrin et al. 2009; Herting et al. 2012; Peper, Cédric and Koolschijn 2012) during adolescence.

The development of female psychology is therefore, to some extent at least, influenced by the girl's hormones.

The Effect of Hormones on Female and Maternal Personality

Here, we describe the feminine particularities of two elements of psychology that develop in

adolescents: empathy and decision-making. Note that cognitive empathy consists of understanding another person's emotions, while emotional empathy consists of sharing their feelings.

Feminine and Maternal Empathy. Adolescence prepares men to become fathers and women to become mothers, roles in which empathy plays a central role. Empathy is more highly developed in species whose offspring are highly dependent on their parents (Waal and Preston 2017). This is the case for the human species. But female and male empathy are different.

S. Baron-Cohen (2004), a British professor of developmental psychopathology, sums up the male–female difference in empathy as follows: The female brain is primarily wired for empathy. The male brain is primarily wired for understanding and constructing systems. This appears to be the source of complementarity between women and men and between mothers and fathers (Christov-Moore et al. 2014). A woman's empathy is said to rely heavily on the activity of mirror neurons: the suffering that a woman sees is inscribed in her brain, almost as if she were the one suffering; this inclines her to respond quickly when she observes suffering. A man's empathy is based more on the neural pathways used for thinking: the response to the suffering of those around him would therefore be less immediate on average, depending on the rational analysis carried out by the man (Schulte-Rüther et al. 2008).

The differences between male and female aptitudes for empathy are present from birth. In maternity wards, for example, it is more girls than boys who cry in response to the cries of other newborns (Hoffman 1977). This is the result of an innate aptitude for emotional empathy. This ability is often highly developed in little girls from an early age. Other aptitudes, more common in little girls than in little boys, contribute to the empathic richness of the female psyche. These include the ability to read the emotional state of those around them in their eyes (Wasserman and Lewis 1985), the ability to use nonverbal language (Berglund, Eriksson and Westerlund 2005), and the ability to remember details of a situation (Cahill 2006).

The onset of adolescence is marked by a rapid increase in the differences between boys and girls in terms of empathy (Herba and Phillips 2004; Lam, Solmeyer and McHale 2012). This is because the quantity and action of the neurotransmitters involved in the empathic process (vasopressin and oxytocin) change according to the level of sex hormones (mainly testosterone, the level of which is much higher in men than in women, and estrogen, the level of which is higher in women and is regulated by the female cycle) (Huber, Veinante and Stoop 2005; Vries 2008; Engel et al. 2019). For women, this translates into a greater ability to perceive feelings in the eyes of those around them than in men.

Decision-Making. Four characteristics of decision-making develop during adolescence, with differences between boys and girls: the role of emotions, risk-taking, intuition, and attention to detail.

The Role of Emotions in Decision-Making. The cerebral amygdala, which plays a central role in managing emotions, develops strongly during adolescence. It functions differently in men and women (Heany et al. 2016). Messages from the cerebral amygdala are transmitted less to the decision-making centers in men than in women. Blocking these messages is one of the ways in which testosterone acts on the male brain. In this way, when it comes to making a decision, a man is partially "freed" from the brake that the weight of emotions can sometimes put on, while a woman remains fully informed of the emotional aspects.

Taking Risks into Account. Young men are less risk-averse than young women (Westlye et al. 2011). So, for example, in a game, while men tend to take risks to obtain a big win, women more often choose successive small wins that are less risky (Dhingra et al. 2021). This difference is partly due to the effect of hormones: while testosterone encourages risk-taking,

estrogen encourages risk avoidance (Forbes et al. 2010; Kurath and Mata 2018). However, it seems that things are more subtle, with women's attitude to risk depending on the area in question. Whatever the case, there is no doubt about the effect of sex hormones on risk management.

Women's Intuition. A study of 949 young people aged between eight and twenty-two (Ingalhalikar et al. 2014), including 521 girls, showed that during adolescence, there are radical changes in the circulation of information in the brain. In girls, exchanges between the two brains predominate. This would seem to be a sign of a great deal of interaction between the rational part of the decision-making process and the intuitive part. In boys, on the other hand, there are more exchanges within the same brain than between the two brains, which is consistent with their greater coordination between what is perceived and what is done, leaving less room for intuition.

More Details. The fourth characteristic of the female decision-making personality is that it takes into account the "details." Women often think more than men about all the intermediate steps required to achieve a goal. This can be explained by their relative aversion to risk and by two aptitudes that are more developed in women: interest and the ability to memorize details, as well as awareness of the successive stages involved in achieving a goal. Interest in and ability to memorize details are often greater in women than in men, who memorize the whole picture more easily. This is an innate difference (Cahill et al. 2004), which is amplified by male and female hormones (Nielsen et al. 2011). Awareness of the successive stages in achieving a goal is activated by information from the cerebral amygdala (Guitart-Masip, Talmi and Dolan 2010; Dolan and Dayan 2013; Leitão, Burckhardt and Vuilleumier 2022). This information is less likely to reach the decision-making centers in the presence of testosterone.

The Gradual Onset of the Female Cycle Gives Young Girls Their Hormonal Profile, Which Differs Considerably from That Established by Hormonal Contraception

The female cycle is established gradually, during the years of puberty and more generally throughout adolescence. The first few years are marked by a balance in favor of estrogen. It is only gradually that a balance between estrogen and progesterone comparable to that in adulthood is achieved.

There are four phases in the development of menstrual cycles (Vollman 1977), which can be identified by observation by the young woman herself:

1. Episodes of mucus discharge at the vulva, without bleeding; this is evidence of episodes ("waves") of development then disappearance ("atresia") of small follicles in the ovary without the quantity of estrogen produced being high enough for bleeding to occur when they disappear: the girl therefore has episodes of low intensity of estrogen secretion, in addition to the other hormonal secretions that have taken place over the previous years in the adrenal glands acting on the brain and the rest of the body (cortisol, androgens, growth hormones).
2. Then, after a few months or more, bleeding occurs, which constitutes the young girl's first "period"; this bleeding is generally not painful as it is simply the consequence of a fall in estrogens after a period of greater estrogen impregnation than previously.
3. Then come the first real periods (bleeding following ovulation), which are sometimes painful; the painful nature of these periods results from a corpus luteum that is still short-lived and secretes little progesterone: progesterone is added to

estrogen, but the balance is still very much in favor of estrogen.
4. Finally, the cycles become more regular, the corpora lutea longer, the periods less painful: the balance between estrogen and progesterone has reached its "adult" level.

The time required to go through these four stages varies from girl to girl. However, all have months or years of equilibrium in favor of estrogen, between the ages of around ten and twelve, and the acquisition of adult menstrual cycles.

For a long time, this period of predominant estrogen secretion in early adolescence was considered simply a sign of immaturity. For many young girls, irregular cycles were a reason for taking hormonal contraceptives. Current knowledge about the role of hormones in the development of female psychology is leading us to reconsider this practice.

Indeed, given the importance of estrogen in brain maturation, it seems very important to consider this installation of cycles, with a predominance of estrogens, as likely to play a part in the construction of the female psyche. This is a serious reason for questioning the use of hormonal contraceptives during adolescence. In fact, as we shall now show, hormonal contraceptives do not replace a young girl's natural hormones.

What Science Tells Us about the Effect of Hormonal Contraceptives on the Brain and Personality

Hormonal contraceptives affect the hormonal balance in two ways: (1) they modify and often cancel out the natural hormonal rhythm; (2) they add artificial hormones that act differently on the brain than natural hormones.

Results of Scientific Studies

Scientific studies compare the abilities of women with and without hormonal contraceptives. The skills most studied are those that show differences between men and women and can be measured with sufficient reliability. These include memory, spatial orientation, and verbal and nonverbal language skills.

Memory. Women are better at remembering details, while men are better at remembering the whole picture. Memory is often enhanced by estrogen (whereas testosterone reduces memory) (Hampson and Morley 2013). For example, women memorize more words during the fertile (estrogenic) phase of their cycle than during other phases (Phillips and Sherwin 1992).

Research on hormonal contraceptives shows that the use of hormonal contraception impairs memory (Kuhlmann and Wolf 2005):

- The memory of women taking hormonal contraceptives varies according to the days of the pill pack (Mordecai, Rubin and Maki 2008) (weaker on inactive pill days—in estroprogestogenic contraceptives, which have twenty-eight pills, seven of which are inactive—stronger on active pill days).
- Under hormonal contraception, on average, women are better at remembering locations (Bianchini et al. 2018), an ability which is usually higher in men (León, Tascón and Cimadevilla 2016).
- Emotional memory under hormonal contraception is closer to that of men than to that of women without hormonal contraception (Wolf et al. 2001; Cahill 2003; Nielsen et al. 2011). Generally speaking, men memorize the whole more than women. Stress reduces overall memory in men and memory for details in women without hormonal contraception. When taking hormonal contraceptives, women are better at remembering the big picture and worse at remembering details.

Ability to Situate Herself in Space. When using hormonal contraception, women's spatial awareness is sometimes better, comparable to

that of men (Wharton et al. 2008). The effect of the pill depends on the progestogen used. When it is androgenic, the ability to situate objects in space is strong, as in men. On the other hand, when the progestogen is antiandrogenic, women are less able to situate objects in space than other women.

Verbal and Nonverbal Language Skills. On average, women have a greater aptitude for verbal and nonverbal language, especially during the fertile period of the cycle. Several facets are involved: some concern language, others face recognition and eye contact. Hormonal contraceptives modify word management skills (Rumberg et al. 2010). They also modify the activity of brain areas involved in recognizing faces (Marecková et al. 2014). These skills contribute to feminine and maternal empathy and are particularly relevant to the female personality.

Hormonal Contraceptives Do Not Replace a Girl's Natural Hormones but Add Hormonal Effects That Affect Her Personality

Hormonal contraceptives all contain progestins and possibly a synthetic estrogen, ethinylestradiol. Ethinylestradiol has a similar activity to natural estrogens. But progestins are very different from natural progesterone. There are two types: those with an androgenic action, and those with an antiandrogenic action (Jung-Hoffmann and Kuhl 1987).

With hormonal contraceptives, variations in blood levels of synthetic estrogens are not identical to variations in natural estrogens. It is not regulated by brain stimuli (follicle-stimulating hormone (FSH) and luteinizing hormone (LH)), unlike what happens in a young girl not taking hormonal contraceptives. In addition, there is no gradual onset of progesterone secretion periods, unlike in girls not taking hormonal contraceptives (Sahlberg, Landgren and Axelson 1987).

Finally, when hormonal contraceptives are used, the natural secretion of small doses of testosterone seen without contraception is reduced (Graham et al. 2007; Hietala et al. 2007). Yet this secretion contributes to a dynamic lifestyle.

Conclusion: What Recommendations Can Be Made following This Review?

We have seen that adolescence is a period when the temperament is structured by a change in the brain under the effect of sex hormones. We then showed how the hormones of the menstrual cycle contribute to feminine brain development. Then we saw that the gradual establishment of cycles during adolescence is the source of an estrogenic climate that has an impact on the psyche. Finally, we presented neuroscience results showing the psychic changes induced by hormonal contraceptives. Hormonal contraception can in particular reduce risk aversion and diminish emotional understanding and empathy.

Although these facts are of paramount importance for the development of female personality, they are little-known in the medical community. It is therefore necessary to disseminate this information within the medical profession. In addition, it is essential to provide young girls and their parents with comprehensive information before prescribing any hormonal contraceptive treatment. This will enable them to make informed decisions.

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