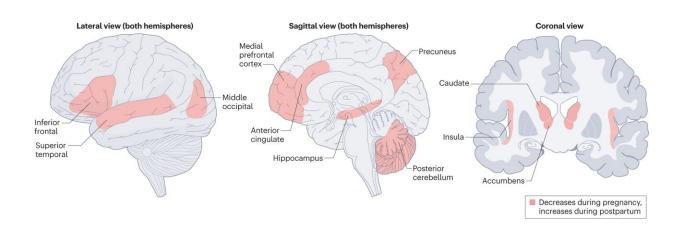


Choreography between hormones and the brain key to understanding how women adapt to motherhood, says study

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Changes in gray matter volume during the transition to motherhood. Shaded areas represent brain regions whose gray matter volume has been reported to decrease during pregnancy and to increase during the postpartum period. Of note, the figure only shows regions where concurrent decreases and increases have been documented, leaving out additional brain regions reported to decrease during pregnancy but not to increase during the postpartum period or vice versa. Credit: *Nature Reviews Neuroscience* (2023). DOI: 10.1038/s41583-023-00733-6

Researchers from the Universitat Autònoma de Barcelona (UAB), the Gregorio Marañón Health Research Institute and the Hospital del Mar Research Institute have published the first paper that reviews the scientific literature on the neurobiological adaptation occurring during



pregnancy and postpartum in humans and other animals.

The article, with Camila Servin-Barthet and Magdalena Martínez as first authors and Òscar Vilarroya and Susana Carmona as senior authors, was published in *Nature Reviews Neuroscience* and will be featured on the cover of the October issue of the journal.

The researchers reviewed a total of 174 articles, in which they analyzed the connections among three fundamental areas: changes in brain structure, hormonal evolution, and maternal behavior, to open new lines of research and advance in women-oriented research.

According to the scientists, all information points to the fluctuation of hormones, mainly related to estrogens, as being what triggers plasticity processes in the brain during a human pregnancy and postpartum period. However, more research is needed to explain what types of plasticity processes (which imply changes in brain cell function, structure, and connectivity) are involved in the transition to motherhood in humans, and how they affect maternal behavior.

Motherhood and morphological changes

Motherhood is a physiologically and psychologically life-changing event, which includes a series of adaptations in how the mother behaves, aimed at ensuring the well-being of her offspring.

Researchers from the UAB and the Hospital del Mar Research Institute were the first to demonstrate in 2017 that a pregnancy implied changes in the brain morphology of first-time mothers, reducing the volume of gray matter in regions involved in social relation, and that these changes were maintained for at least two years after giving birth. Since then, researchers have observed that the brain's gray matter changes in volume in the different stages of maternity and postpartum and that it is always



accompanied by extreme hormone fluctuations.

In the article, researchers describe for the first time three fundamental factors in understanding the adaptation to motherhood in humans. First are estrogens (oestradiol), as the main hormone candidates in inducing changes in the brain. Second is the brain circuit related to social cognition (involving the medial frontal cortex and precuneus, as well as other areas), as the specific region in which these changes take place. And third, there are the psychological changes, i.e., the cognitive and emotional processes necessary to develop a mother-child relationship that adapts to the different phases of pregnancy and postpartum. This third factor is what most differentiates humans from other animals and little is known about it.

Roadmap for future research

Based on the evidence published, the researchers point out which neuroplasticity processes most likely contribute to the changes identified, and how these can be related to pregnancy and maternal behavior hormones. They also prepared a roadmap with different lines of research to advance the study of human adaptation to motherhood.

One first line of research should focus on identifying brain cell substrates. According to the experts, it is improbable that the large-scale dynamics of changes in gray matter at morphological and molecular levels be produced exclusively by plasticity. In rats, researchers observed that hormonal fluctuation, particularly at the end of the pregnancy, affects the plasticity of neurons and microglia, with a greater proliferation of this latter cell type.

A second line should work towards describing the mechanisms by which sexual hormones, especially estrogens, bring on the changes detected in structural and behavioral reorganization. Given the hormonal



environment existing during the pregnancy and postpartum period and the interactive nature of these molecules, it is most likely that these changes are the result of a complex exchange of steroids and hormonal peptides. To understand this role better, research must be conducted on a greater number of hormones and metabolites, with special attention put on oxytocin and prolactin.

The third challenge focuses on identifying the psychological evolution occurring during pregnancy and postpartum and characterizing the functional changes in the brain responsible for the development of human conduct. In studies with rats, molecular and morphological changes were observed accompanied by the emergence of maternal behavior, but not so in humans. Not only that, but the association between neuroanatomic changes and different aspects of maternal behavior in humans are few and difficult to replicate.

Improving the methodology in MRI studies in humans and questionnaires will allow us better to infer the link between the brain changes observed and the different components of maternal behavior. All this while bearing in mind extrinsic postpartum factors, which could induce changes in the circuits related to maternal care.

A scarce number of studies conducted on women

Most studies conducted up to date have used rats. That is why the researchers put emphasis on the importance of developing research studies on women. "There are coincidences between humans and other animals, but there are many cerebral differences, particularly on the cerebral cortex, the most evolved part of the brain, and hormonal differences, given that the choreography between sexual hormones is different in each species," explains Camila Servin, researcher from the UAB Department of Psychiatry and Legal Medicine and at the Hospital del Mar Research Institute.



"Until 2017 we had not begun to study changes in the brain occurring during pregnancy, and until now very little has been studied on the role of hormones and the psychological environment," explains Oscar Vilarroya, researcher from the UAB Department of Psychiatry and Legal Medicine and at the Hospital del Mar Reseach Institute. "Surprisingly, the study of what is one of the most generalized and important human experiences has never taken central stage," the neuroscientist concludes.

More information: Camila Servin-Barthet et al, The transition to motherhood: linking hormones, brain and behaviour, *Nature Reviews Neuroscience* (2023). DOI: 10.1038/s41583-023-00733-6

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