

The “Choreography” between hormones and the brain key to understanding how women adapt to motherhood

- Researchers from the UAB, the Gregorio Marañón Health Research Institute, and the Hospital del Mar Research Institute have published the first article reviewing research conducted to date on the neurobiological adaptation of women to motherhood by analysing the relation of hormones, brain and behaviour during pregnancy and the postpartum period.
- The findings support the hypothesis that fluctuating hormones, mainly estrogens, are related to changes in the human brain structure, but what is yet to be determined is how this influences neuroplasticity and maternal behaviour.
- The article sets a roadmap for future research projects and demonstrates the scarcity of research conducted until now in women, essential due to the differences existing in the sexual hormones of each species.

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 existing until now 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*.

The researchers reviewed a total of 174 articles, in which they analysed the connections among three fundamental areas: changes in brain structure, hormonal evolution, and maternal behaviour, 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 behaviour. **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 grey 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 grey 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 behaviour 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 grey 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 behavioural reorganisation. 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 characterising 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 behaviour, but not so in humans. Not only that, but the association between neuroanatomic changes and different aspects of maternal behaviour 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 behaviour. 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 Òscar Vilarroya, researcher from the UAB Department of Psychiatry and Legal Medicine and at the Hospital del Mar Research Institute. “Surprisingly, the study of what is

one of the most generalised and important human experiences has never taken central stage”, the neuroscientist concludes.

Also participating in the paper were researchers from the Biomedical Research Networking Centre in Mental Health (CIBERSAM) and from Ohio State University.

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Images:

<https://drive.google.com/file/d/137DI1P1MBsJmHwKQun5NCLkkxsgBmA8f/view?usp=sharing>

Experts team of the Cognitive Neuroscience Research Unit (URCN) of the UAB's Department of Psychiatry and Legal Medicine.

https://drive.google.com/file/d/1_qUrd90h7yFk0KOUXyLJNtuvFFp88Cla/view?usp=sharing

The researchers Susana Carmona and Magdalena Martínez-García, from the Instituto de Investigación Sanitaria Gregorio Marañón.