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Brain changes during pregnancy might help parents to bond with their children after birth.

HOW PREGNANCY CHANGES THE BRAIN

It's a transformational time long neglected by neuroscience. That is starting to change. **By Liam Drew**

In November 2008, neuroscientist Susana Carmona – then a postdoc studying attention deficit hyperactivity disorder – was driving two colleagues to a party when one of them revealed that she was thinking about having a child. The trio became so engulfed in conversation about how pregnancy might change her brain that they diverted from the party and headed to their laboratory to search the literature.

They found numerous studies in rodents, but in humans, "there was basically nothing at all", says Carmona.

Shocked by this gap in research, Carmona and her colleagues convinced their mentor at the Autonomous University of Barcelona, Spain, Oscar Vilarroya, to let them run a study using magnetic resonance imaging (MRI) to measure the neuroanatomy of women before they became pregnant, and then again after they gave birth.

Squeezed in alongside their main projects, the investigation took eight years and included dozens of participants. The results, published in 2016, were revelatory[1]. Two to three months after giving birth, multiple regions of the cerebral cortex were, on average, 2% smaller than before conception. And most of them remained smaller two years later. Although shrinkage might evoke the idea of a deficit, the team showed that the degree of cortical reduction predicted the strength of a mother's attachment to her infant, and proposed that pregnancy prepares the brain for parenthood.

Today, Carmona, now at the Gregorio Marañón Health Research Institute in Madrid, is one of several scientists uncovering how pregnancy and parenthood transform the brain. Elseline Hoekzema, one of Carmona's passengers that evening in 2008, is another. In 2022, Hoekzema, who is now at the Amsterdam University Medical Centre in the Netherlands,

confirmed that the cortical regions that shrink during pregnancy also function differently for at least a year after giving birth[2].

These studies and others, say researchers, highlight a transformational life event that has long been neglected by neuroscience — one that around 140 million women experience annually.

"There's a lot of attention paid to pregnancy, but mostly in terms of the body and making the pregnancy successful," says Liisa Galea, a neuroscientist at the University of Toronto in Canada. Only 0.5% of published human neuroimaging studies have looked at health factors specific to women.

Yet, the stereotypical idea of 'pregnancy brain' is pervasive across many societies. Surveys show that 50–80% of people who have been through pregnancy and birth report memory deficits, 'brain fog' or other cognitive issues. "People really want to know what's happening to their brains and to their minds," says Winnie Orchard, a neuroscientist at Yale University in New Haven, Connecticut.

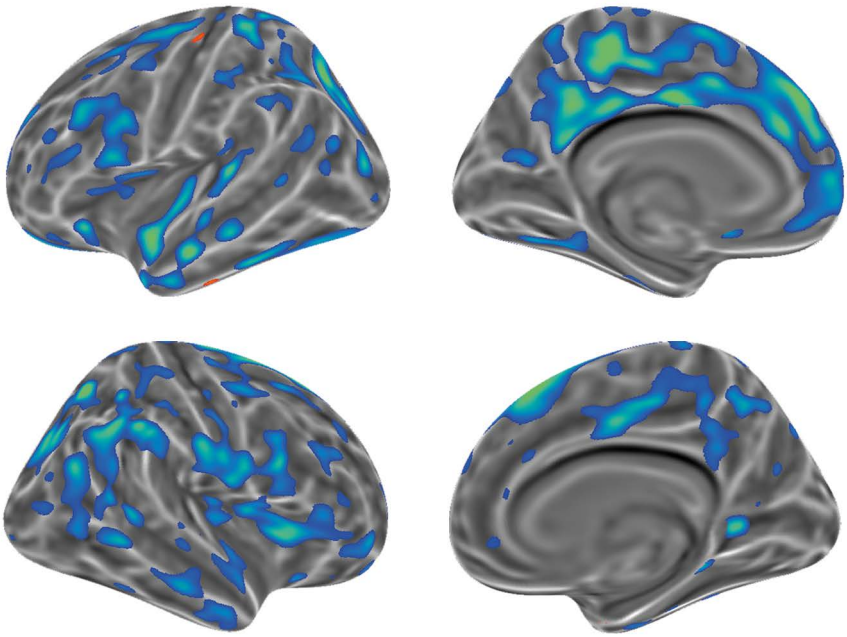
Several longitudinal brain-imaging projects are under way, but the field is in its infancy. "We're still in the early days," says Hoekzema. "We've seen strong brain changes but are only beginning to scratch the surface of what this means for a mother."

Life transition

Pregnancy and its hormonal surges alter physiology hugely. "Pretty much every single system in the body is hijacked to allow for the fetus to grow," says Galea. In animals, these hormones have been shown to transform the brain and behaviour. Virgin female rats, for example, typically ignore rat pups or kill them[3]. But injecting the animals with pregnancy-mimicking hormones leads them to behave like mothers, grooming and protecting pups.

Studying the biological effect of pregnancy is considerably more complex in people. The behavioural changes in humans are much less stark, and pregnancy's physiological upheavals coincide with substantial psychosocial and environmental changes. "Disentangling all of these pieces is really quite complicated," says Orchard. Examples of changes to biology that are independent of pregnancy come from new fathers, she says, who also experience hormonal changes and brain alterations[4] that partially tally with those seen in mothers. These changes are greater the more care they provide.

Using an appropriate comparison group is therefore essential — be that fathers, non-biological mothers or non-female birthing parents. Hoekzema and Carmona's first study compared gestational mothers with new fathers, and Carmona earlier this year compared gestational and non-gestational mothers in lesbian couples[5]. Although there are subtle changes to the brains of non-gestational parents, they are dwarfed by those seen in pregnant people.



During the third trimester of pregnancy, some parts of the cortex reduce in thickness (blue).

M. PATERNINA-DIE *ET AL./NATURE NEUROSCI.*

The changing brain

The rule seems to be that any brain region that changes size during pregnancy shrinks. Numerous brain structures are affected, including the ventral striatum, which is involved in reward processing, and the hypothalamus, which is instrumental in controlling instinctive behaviours. The hippocampus, a structure essential for memory, also transiently shrinks during gestation.

But the impacts are largest in the cerebral cortex — particularly, Hoekzema says, in areas that integrate information from other regions of the brain, "where we differ most from other animals".

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In their 2016 paper, Hoekzema and Carmona showed that the changes seen shortly after birth mainly affected a circuit called the default mode network. This network, Hoekzema says, "is involved in social processes such as theory of mind and empathy; in thinking about and understanding others and yourself".

In a preprint this year[5], Carmona's group refined this result by taking MRI scans of women during pregnancy, as well as before and after. (In the past, ethics review boards have been wary of sanctioning clinically unnecessary scans.) Data from the second and third trimesters revealed that the entire cortex shrinks by nearly 5% across pregnancy.

After birth, most changes quickly and fully reverse — except in the default mode network. There, Carmona says, "the recovery is different and potentially it does not reach pre-pregnancy levels".

These alterations are probably driven by hormones. Hoekzema[2] and Carmona[5] have independently observed that the magnitude of neuroanatomical changes correlates with levels of oestrogen and related hormones.

But what do these changes mean for behaviour? Accumulating data show that the degree of change in the default mode network correlates with the strength of the mother–infant attachment, maternal responses to infant pictures and nesting behaviours — and inversely with problems in the bonding process. Those links make sense, Hoekzema says, given the network's role in social processes such as empathy and theory of mind.

To some, it's intuitive to think of shrinkage as a deficit, says Galea, whereas all it truly signals is a change. Hoekzema says that research on neural metabolites indicates it's unlikely that neurons are being lost. And most researchers favour the view that shrinkage reflects a refinement of neural functions.

This suggests that the processes of gestation and giving birth induce a neurodevelopmental transition — akin to the hormonally driven

MRI scans can show how the brain changes during pregnancy and after birth.

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brain changes that accompany adolescence. Indeed, both life phases are marked not just by cortical shrinkage, but also by a flattening of the cortex's folded surface. These changes might allow the individual to transition to a new stage of life — in adolescence, into independence; after pregnancy, into having someone depend on you.

Wider impacts

Alongside adaptations directly related to infant care, there are questions about how pregnancy influences cognition more generally. In 2023, when Orchard reviewed this topic, she encountered a potpourri of isolated studies[6]. "Different studies have chosen different time points, different cognitive tasks or different comparison groups," she says.

Memory deficits, however, are consistently observed during the third trimester[7]. These might be linked to decreases in hippocampal volume, but they are rarely clinically significant or detrimental to daily life, Orchard says.

Post-partum data are much less conclusive. "Some studies show deficits. Some studies show no differences. Some studies even show some enhancements," Orchard says. One skill that might get a boost is executive function, a high-level process that is important in self-regulation and managing competing cognitive demands.

Where this leaves the 'pregnancy brain' idea is complicated. Confirmation bias might lead some people to think that their brain function is worse than it really is when they have a forgetful moment. But new mothers are typically operating under considerable cognitive burdens and performing many new mental tasks well.

Orchard has found that a year after giving birth, mums that subjectively reported cognitive deficits showed no difference in lab tests compared with non-mothers[8]. But, she says, "just because we couldn't find it, doesn't mean that it's not there".

A vulnerable time

One issue that definitely applies to the period of pregnancy and early parenthood is the heightened risk of mental-health issues.

Worldwide, postpartum depression affects 17% of new mothers — with the highest rates occurring in low- and middle-income countries. Psychosis and obsessive–compulsive disorder also occur at elevated frequencies, although their absolute prevalence is very low.

Again, hormones are one likely culprit. It's well known that progesterone falls precipitously at birth, but it was only last year that the first oral treatment for postpartum depression, zuranolone, was approved in the United States. Zuranolone mimics a progesterone relative, and acts on receptors in the brain to help regulate mood.

Galea says that many pregnancy-related physiological changes — from hippocampal shrinkage to neurochemical and immunological changes — mirror changes seen in depression generally. "It's like a perfect storm."

Carmona thinks that large, long-running studies that deeply characterize the many facets of pregnancy and beyond — involving brain imaging, monitoring hormone levels and immune factors, and psychosocial data — could shed some light. Other studies could recruit even larger numbers of less intensively studied volunteers to define how key factors vary across populations.

Some of these samples are bound to include people with depression, and potentially other psychiatric issues, as well as people experiencing difficulties in bonding with their baby. This will hopefully reveal telling correlates of negative outcomes. "That's like the end of the whole story," Carmona says, "to try to move this to clinical practice."

Meanwhile, researchers have discovered an upside to having a baby that they are keen to explore more. In the long term, it might keep the brain younger. In 2019, Ann-Marie de Lange, who studies ageing at Lausanne University Hospital in Switzerland, took brain-scan data from around 12,000 middle-aged women enrolled in the UK Biobank project. Happy to find that this data set, unlike many others, included parental status, de Lange asked whether the women's brains varied according to how many children they had had.

Using algorithms that convert neuroanatomical data into a brain-age score, de Lange found that mothers' brains looked, on average, around 7 months younger than those of women without children[9]. A separate study posted as a preprint in May supported the finding, showing that the brains of middle-aged parents — irrespective of sex — seem younger functionally, with better-connected regions the more children they had had[10].

De Lange says that these results suggest that the neuroplasticity of pregnancy "could be a boost to the brain".

The studies underscore an important message of this emerging field: that biomedical research should routinely factor in reproductive histories, because having a child has acute and long-term impacts on the brain.

More immediately, researchers argue for social policies that take into account the remarkable neuroplasticity of this period, such as the need for lengthy paid maternity leave. "When we're thinking about neural adaptation and a time of great change," Orchard says, "we need to acknowledge that change takes time, and it is a vulnerable period."

Establishing a research field also takes time. But 16 years on from that fateful conversation in her car, Carmona is looking forward to a more informed future. "I have faith," she says, "that we will find very, very interesting things in the next decade."

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