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How does pregnancy change mothers' behavior?

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Abstract

Pregnancy changes a lot of things in a mother: the body goes through many transformations trying to adapt to the needs of the baby. The mother's behavior changes as well, as she has to care for her newborn. There is some indirect evidence that the baby (through its genes) could instruct the mother's brain and alter her behavior even before it is born. But is this really true? We have previously found a gene which controls the amount of hormones produced by the *placenta*, an organ that connects the developing embryo to the mother. To test if the embryos could affect the mother's behavior, we conducted a series of experiments on mice who were pregnant with embryos expressing different doses of this gene. Indeed, mothers exposed to higher doses of the gene preferred nest building over baby nursing.

Introduction

We all inherit two copies of our genes: one from our mother and one from our father. Usually both of these copies, also called *alleles*, are active. Sometimes, though, only one copy is active and the other one is silenced. This evolutionary phenomenon is called *genomic imprinting* and many researchers believe it evolved in mammals as a battle between the sexes – males want their offspring to grow and be stronger at the expense of the mother and her care, while the mother prefers to save resources for herself so that she can have other children in the future.

During pregnancy hormones are known to affect both the body and the behaviour of the mother. A gene called *Phlda2* controls a little understood group of hormones, produced by a specific part of the placenta (Figure 1). We have previously shown that *Phlda2* regulates the size of this placental part in a negative manner. That means the more the gene is *expressed*, the less the placental part grows (and the less hormones it produces).

This gene is subject to genomic imprinting: one of its copies is usually silenced – the father's copy. That means only one allele of the gene is active, which leads to a bigger size of the placental part that produces hormones (in contrast to when both alleles are active and make it grow less). This can be thought of as a struggle between the genes over maternal resources. Does this mean that the father and the father's genes control how well the mother cares for their baby through those hormones? That's want we wanted to find out.

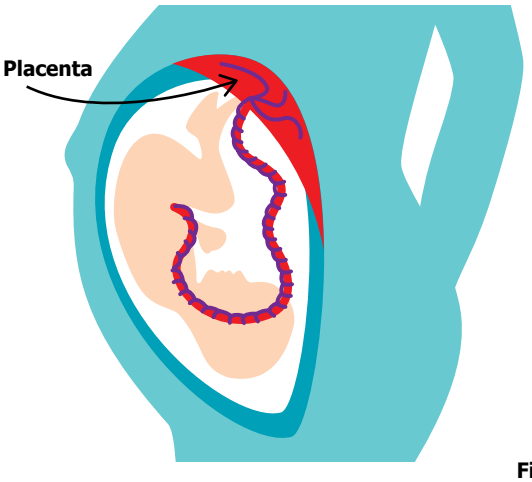

Figure 1:
The placenta connects the developing embryo with the mother so it can get all the food it needs to grow.

Methods

We used mice with different *genotypes* to produce various embryos:

- Mice who had both copies of *Phlda2* present, with the father's copy inactive (*wild type*)
- Mice who had neither copy of the gene present
- Mice who overexpress the gene *Phlda2* (both copies active)

After the mice mated with each other, we transferred their embryos only to female wild type mice. This way we could see how embryos (and their placenta) with the different genotypes – and thus different expressions of *Phlda2* – affect the wild type mothers.

The mothers were placed in three groups depending on the embryos they were carrying:

- Mothers carrying wild type embryos (1x)
- Mothers carrying embryos with loss of the gene's function (0x)
- Mothers carrying embryos with overexpressing *Phlda2* gene (2x)

First we wanted to see if there is a change in the different mothers' brains during pregnancy. We assessed this by examining their *hypothalamus* and *hippocampus* via *microarray analysis*.

We then analyzed the mothers' behavior after giving birth:

1) We used an *elevated plus maze* to see if they were anxious.

2) We observed if the mothers were more active at day or at night (when they give milk they are usually more active during the night).

To analyze the maternal care we observed:

1) how long it took for the mothers to sniff their babies for the first time,

2) how long it took for the mothers to retrieve their babies (Figure 2), and

3) whether the mothers spent more time building the nest or nursing (feeding) and grooming (cleaning) the babies.

Figure 2:
An example of a basic pup retrieval protocol.
1. Location of pups and nest before retrieval.
2. Two pups that have been retrieved and returned to the nest.
3. No pups have yet been retrieved but one is nearly into the heart of the nest.
4. A failure to retrieve pups

Results

We did notice an important change in the brains of two groups of mothers: the ones carrying 0x embryos (without expression of *Phlda2*) and the ones carrying 2x embryos (overexpression of *Phlda2*) both had altered genes linked to smell in two important areas of their brains. Smell is a sense which is important for the recognition of their babies.

Analyzing the mothers' behavior and their care for their babies showed us the following (Figure 3):

- The three groups of mothers didn't show any differences in their anxiety.
- The time for the first sniff of the babies was the same for each group of mothers.
- Mothers with 1x babies (expressing 1 copy of *Phlda2*) were more active during the night – which is normal – while the other two groups of mothers were not.
- Mothers who carried embryos with no *Phlda2* expression (0x) took much longer to retrieve their babies, but they nursed their babies a lot more often.
- Mothers who carried embryos with overexpressing *Phlda2* (2x) were the best at building nests.

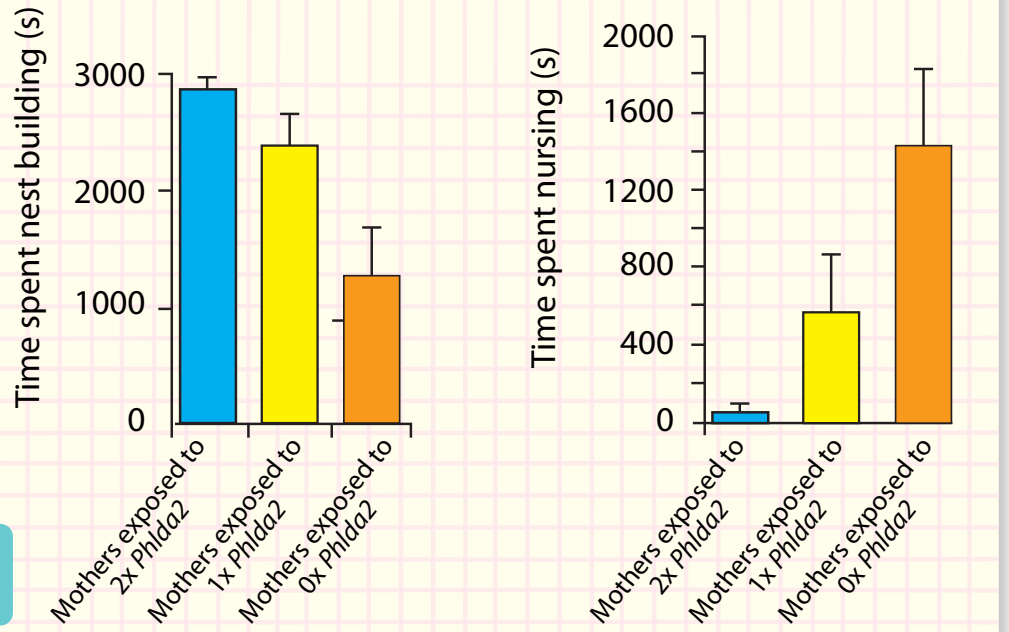

Figure 3:
Priorities of the mothers exposed to different doses of *Phlda2* during nest building.

How do lower doses of *Phlda2* affect the mothers' behavior?

Discussion

In mammals, mothers are the primary caregivers while males are rarely involved in the care of the offspring. This has led to a conflict between their genes. If the father's genes prevail, there is increased maternal care and investment. If the mother's genes prevail, she will try to preserve herself for any future children. Consistent with these predictions, we observed that the mothers exposed to the lowest dose of *Phlda2* (0x) spent more time nursing and grooming their babies. In contrast, mothers exposed to the highest dose of *Phlda2* (2x) focused more on nest building.

But does this mean that the babies have programmed the mothers to care for them before their birth? Or could the babies have influenced their mothers right after birth?

We can be sure of our results because we provided mothers exposed to either 1x or 0x *Phlda2* with wild type babies from another mother. If the embryos programmed the mothers during the pregnancy, the mothers would still care for the babies even if they were not her own. That was indeed the case: mothers exposed to 0x *Phlda2* nursed wild type babies more often than mothers exposed to 1x *Phlda2*, meaning the embryos (and their father's imprinted genes) altered the mothers' priorities and made these mothers better caregivers

Conclusion

Have you ever wondered how tall you will be? Or what determined the color of your eyes? It's all in the genes. It's all because of your parents. And their parents, and so on. And it's what you will pass on to your children - a big web of interspersed genes. Can you think of an example of what you got from your mom? And from your dad? There are some genes, like *Phlda2*, that are imprinted and that means their expression is controlled by external factors. These genes are important because they can determine key developmental and behavioural outcomes in children. The levels of expression in the placenta is affected by diet and exercise, so it is very important to look after yourself and eat healthy food as much as possible – especially if you want to have kids of your own when you are older!

Glossary of Key Terms

Allele – a variant form of a gene.

Genomic imprinting – when one allele of a gene (the father's or the mother's) is switched off, instead of them both working simultaneously.

Genotype – the set of genes in our DNA.

Elevated plus maze – a test which measures anxiety in animals. The apparatus have two open and two enclosed arms. If the mouse spends more time in the open space it's less anxious, but if it stays in the enclosure it's more anxious.

Expression of genes –when cells use the information from a gene to create the gene product (usually a protein).

Hippocampus –a part of the brain responsible for memory, learning, and responses to fear and stress.

Hypothalamus – a part of the brain responsible for the onset, maintenance and regulation of maternal behavior (among other things).

Microarray analysis – method used to detect the expression of thousands of genes at the same time.

Placenta – an organ which connects the developing embryo with the mother, allowing the embryo to eat, grow, and so on.

Wild type – the typical form of a species (or genes) as it occurs in nature.

REFERENCES

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What is imprinting?
https://learn.genetics.utah.edu/content/epigenetics/imprinting/

Check your understanding

1 What is genomic imprinting?

2 What does the gene *Phlda2* do?

3 Lower doses of *Phlda2* do what to the placenta?

4 Lower doses of the gene do what to the mother?

5 Is genomic imprinting in this case in favor of the father or the mother?