The effect of gut microbes on the mouse brain depends on both sex and stage of development

May 2 2018

A*STAR researchers have shown that the bacteria in the gut can affect the microglia in a mouse's brain. Credit: KATERYNA KON/SCIENCE PHOTO LIBRARY

Immune cells in a mouse's brain react differently to changes in gut-dwelling bacteria depending on whether the mouse is male or female and whether it is a fetus or an adult, A*STAR researchers have found. This discovery has potential implications for brain development and disorders.

Recently, scientists have found increasing evidence that the microbes in our digestive system, collectively known as the microbiome, can affect

the brain via the metabolic products they produce.

Now, Florent Ginhoux from A*STAR's Singapore Immunology Network and an international team of researchers have found that this influence goes all the way back to the womb. By performing microscopy and genomic analyses, they have shown that, in mice, the absence of a microbiome in a mother affects the microglia, one of the major immune cell populations of the central nervous system, of her developing fetuses.

"This was really dramatic," says Ginhoux. "We never thought that a fetus , which is inside a mother, would be affected by her lack of a microbiome. We had previously believed that the brain of a fetus is a closed system, not subject to perturbations, and that it was only when the fetus goes out of the womb, that the environment can influence it."

This effect on microglia was much more pronounced in male fetuses than female ones. Conversely, in adult mice, females were more sensitive than males to the absence of the microbiome or its depletion through the use of antibiotics.

The scientists are as yet unsure what is causing this difference. "At this stage, there is no really clear mechanism that explains why males are so sensitive to this change," says Ginhoux. "We think there may be a crucial window of development during which cells are very sensitive to changes in the environment, which is here exemplified by the absence of the microbiome."

But these differences are highly suggestive since men are known to be more susceptible than women to disorders such as autism, and the early onset of schizophrenia, both of which are thought to originate from dysregulated development in fetuses or early in life. On the other hand, women are more likely to suffer from depression and autoimmune diseases such as multiple sclerosis, which can develop in teenagers or

adults.

The team intends to look at subtle changes to the microbiome that more accurately reflect those likely to occur in real life. They also plan to investigate how different treatments, such as antibiotics or changes to diet, can modulate microglia identity and function during pregnancy and adulthood.

More information: Morgane Sonia Thion et al. Microbiome Influences Prenatal and Adult Microglia in a Sex-Specific Manner, *Cell* (2017). DOI: 10.1016/j.cell.2017.11.042

Provided by Agency for Science, Technology and Research (A*STAR), Singapore