Motherhood permanently alters the brain and its response to hormone therapy later in life

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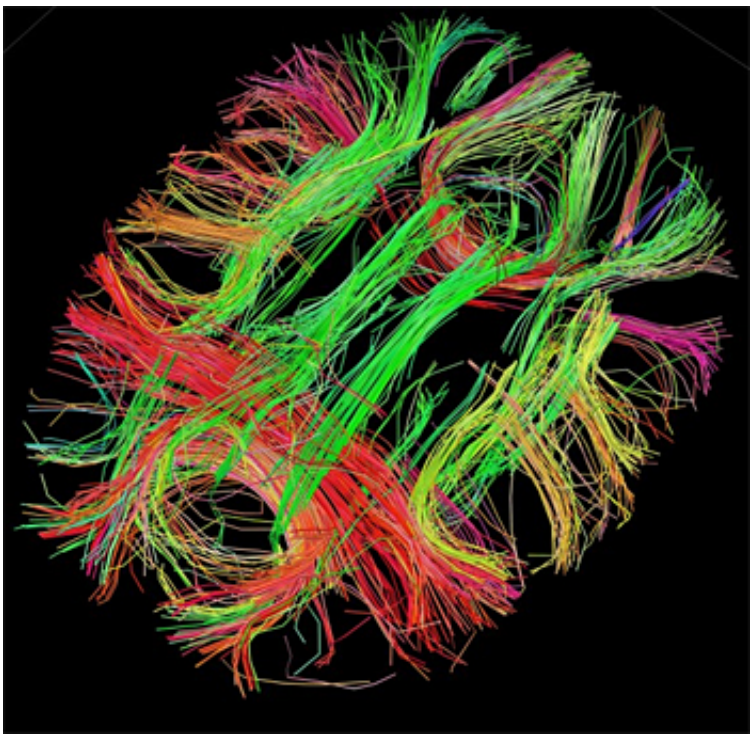

White matter fiber architecture of the brain. Credit: Human Connectome Project.

Hormone therapy (HT) is prescribed to alleviate some of the symptoms of menopause in women. Menopausal women are more likely to be diagnosed with Alzheimer's disease but not other forms of dementia, and HT has been prescribed to treat cognitive decline in post-menopausal

women with variable degrees of effectiveness. New research by Dr. Liisa Galea, at the University of British Columbia, suggests the form of estrogens used in HT and previous motherhood could be critical to explain why HT has variable effects.

Research in women, and Dr. Galea's research in animals, shows that one form of estrogens, called estradiol, which is the predominant form of estrogens in young women, had beneficial effects, while estrone, which is the predominant form of estrogens in older women, did not. Furthermore, the effects of estrone also depended on whether the rats had experienced motherhood: estrone-based HT impaired learning in middle-aged rats that were mothers, while it improved learning in rats that were not. Dr. Galea's latest results were presented at the 9th Annual Canadian Neuroscience Meeting, on May 25th 2015 in Vancouver British Columbia.

"Our most recent research shows that previous motherhood alters cognition and neuroplasticity in response to hormone therapy, demonstrating that motherhood permanently alters the brain" says Dr. Liisa Galea.

Dr. Liisa Galea is interested in how hormones affect brain and behaviour. Hormone therapy (HT) has been shown to have variable effects on brain function and Dr. Galea noted that one factor that had not received much attention was the form of estrogens used in HT. There are three forms of estrogens: estradiol, estrone and estriol. Estradiol is the most potent of estrogens, and it is the predominant form in young women, while estrone is a weaker estrogen and is the predominant form in post-menopausal women. A systematic review of the published scientific literature indicates that estradiol-based HT may have more beneficial effects, while estrone-based HTs may have more detrimental effect on cognition and dementia risk in women.

Dr. Galea studied how two forms of estrogens, estradiol and estrone, affect neuroplasticity, which is how neural pathways in the brain change in response to various factors. Her studies focused on a specific brain region, called the hippocampus, which has important roles in memory and spatial ability, such as navigational skills. Both forms of estrogens increased the production of new cells in a part of the hippocampus called the dentate gyrus in young females. However, only chronic estradiol, but not chronic estrone, significantly increased the survival of these new neurons, and increased the expression of zif268, a protein involved in neuroplasticity.

Chronic estradiol, but not chronic estrone, also improved performance of young female rats in a behavioural test called the water maze. The water maze is a test of memory and orientation in which rats must find a submerged platform in water that they cannot see; they must instead rely on cues located around them to orient themselves and swim to the platform. Rats receiving estradiol based HT found the platform significantly better that rats receiving estrone-based HT.

Finally, Dr. Galea's previous research had shown that motherhood causes changes in the architecture of connections in the hippocampus, so her team investigated whether the different forms of estrogens could have different effects on rats that had experienced motherhood once (primiparous rats) and on those who had not (nulliparous rats). They found that estrone-based HT improved learning in middle-aged nulliparous rats, but impaired learning in primiparous rats of the same age. These primiparous rats also showed a reduction in neurogenesis and zif268, a protein involved in neuroplasticity in the hippocampus.

As estrone is a component of the most common form of HT prescribed for women in the US, these findings could have implications for the treatment of age-related neurodegenerative disorders in women.

"Hormones have a profound impact on our mind. Pregnancy and motherhood are life-changing events resulting in marked alterations in the psychology and physiology of a woman. Our results argue that these factors should be taken into account when treating brain disorders in women" concludes Dr. Liisa Galea.

Provided by Canadian Association for Neuroscience

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