The brain may show signs of aging earlier than old age

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A new study published in *Physiological Genomics* suggests that the brain shows signs of aging earlier than old age. The study found that the microglia cells—the immune cells of the brain—in middle-aged mice already showed altered activity seen in microglia from older mice.

Parkinson's, Alzheimer's and other aging-related neurodegenerative disorders are associated with excessive inflammation in the brain. Scientists believe that overactive microglia cells contribute to the excess inflammation. Normally, microglia protect the brain from infection and ensure the brain functions properly. Their immune response is tightly controlled. Microglia produce pro-inflammatory molecules to turn the inflammation process on, followed by anti-inflammatory molecules to turn inflammation off. With aging, microglial cells can overreact, and their immune activity can become less controlled—they turn inflammation on too quickly or turn it off too slowly. The prolonged or constant inflammation that results can damage the brain.

While it is known that microglia immune activity changes with aging, which response is affected first—the pro-inflammatory or the anti-inflammatory—or, more importantly, when microglial aging begins is not clear, says Jyoti Watters of the University of Wisconsin-Madison and lead investigator of the study. "We show in a mouse model that it may begin earlier than we thought," Watters says.

The research team at the University of Wisconsin-Madison studied the microglia activity of young (two months old) and middle-aged (nine to 10 months old) mice. The researchers injected the mice with lipopolysaccharide, a molecule found in bacteria that strongly activates the immune system and causes inflammation. The mice were injected twice to assess the microglia's ability to reset their immune activity and respond to another bout of inflammation.

The researchers found that middle-aged mice displayed exaggerated pro-inflammatory responses after the first injection. However, anti-inflammatory responses were normal. After the second injection, both pro-inflammatory and anti-inflammatory responses were normal. The data suggest that at middle age, the microglia already showed signs of an altered immune response. But not everything is impaired: The microglia of the middle-aged mice still responded normally to the second injection. "At this time, age-related alterations may only be beginning since other critical capacities have not begun to deteriorate yet," according to Watters. "Of course, it is not known when aging-associated changes in microglial activities begin in the human brain, but these results in mice suggest that it may be earlier than we had previously appreciated," Watters says.

More information: Maria Nikodemova et al. Age-dependent differences in microglial responses to systemic inflammation are evident as early as middle age, *Physiological Genomics* (2016). DOI: 10.1152/physiolgenomics.00129.2015

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