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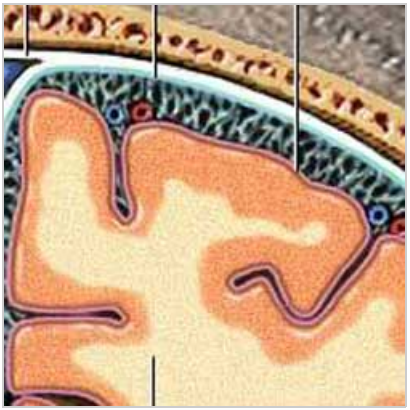
How the immune system's T cells seem to improve learning

By Katherine Harmon



The immune system's cells work hard to fight off infections. But new research is uncovering their important role in cognition, and a study published online May 3 in *The Journal of Experimental Medicine* reveals how the immune system's T cells, which aren't present in the brain, can impact learning and memory.

Inflammation around the brain can hamper thinking, and attacks by inflammatory immune cells have been linked to declines in cognitive ability in patients who have, for example, multiple sclerosis or dementia. "Unexpectedly, however, T cells were recently shown to support learning and memory, though the underlying mechanism was unclear," wrote the study's authors, led by Noël Derecki of the Department of Neuroscience at the University of Virginia in Charlottesville.

To uncover the mechanisms at work, Dereki and colleagues set out to determine why mice deficient in T cells performed poorly in maze learning tests even though T cells themselves are not normally found in the brain and are generally involved with inflammatory responses.

The answer lay in a series of interactions that involves the meninges, or the membranes that surround the central nervous system, where T cells have been shown to congregate after maze training in mice.

Of particular interest to researchers were T cells that make the immune protein IL-4, a cytokine that inhibits other compounds that encourage swelling. When these T cells had been knocked out of mice, the area around the brain and central nervous system had more myeloid cells, which seem to spur inflammation and impair learning.

To test this protein's role in overall ability to learn and remember a task, researchers engineered mice without IL-4 and tested them in the maze against normal mice. The mice that didn't have the cytokine had increased inflammation from myeloid cells in the meninges and "exhibited an astonishingly severe phenotype of impaired cognitive function," noted the researchers. But when these deficient mice were given an injection of normal T cells from their

healthy counterparts, they started to do much better at the maze tests, perhaps because the T cells produced IL-4, which couteracted the inflammation-producing myeloid cells.

"These results represent a major paradigm shift in the understanding of the role of T cells in the maintenance of the delicate pro- and anti-inflammatory balance" in the area surrounding the central nervous system, the researchers wrote. For patients whose cognitive decline is thought to stem from T cell-driven inflammation, the findings suggest that removing T cells from the meninges might spur even more inflammation and worsening conditions. And that understanding could help develop better treatments for people who have weakened immune responses.

Image of meninges layers that surround the brain courtesy of Wikimedia Commons

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