

Discovery opens new approaches to neurological diseases

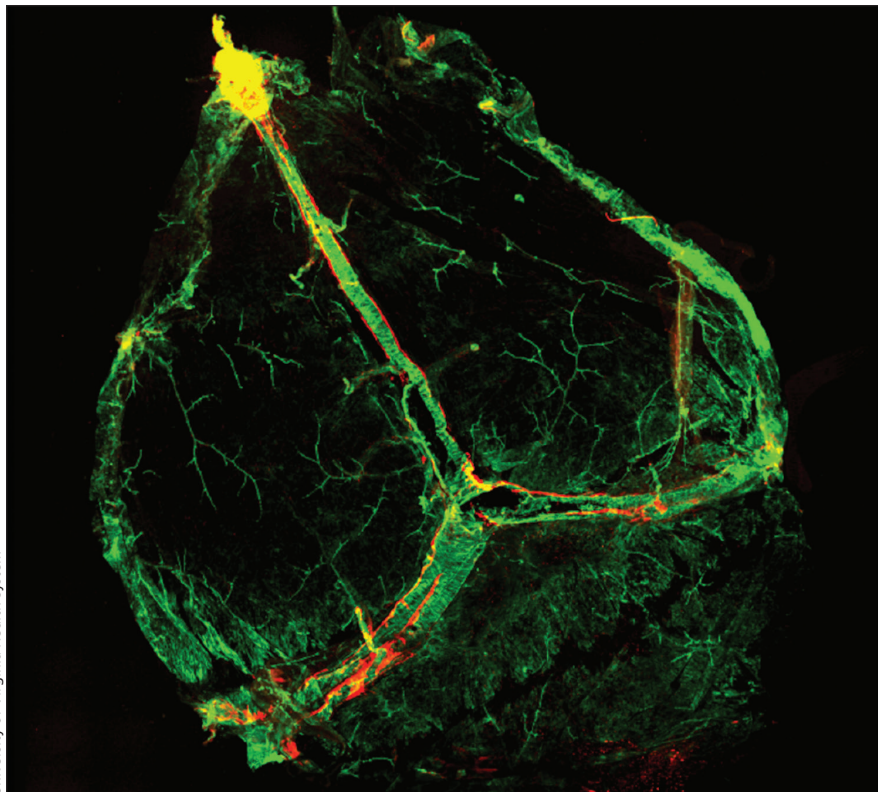
The serendipitous discovery of lymphatic vessels in the brain is a key piece of the puzzle in understanding immune processes in the nervous system, and will shed new light on the causes and treatment of neurodegenerative diseases such as multiple sclerosis (MS), Alzheimer disease, Huntington disease and amyotrophic lateral sclerosis (ALS).

“Every textbook that has ever been written will say there is no lymphatic system in the brain,” explains principal author Antoine Louveau, a postdoctoral fellow at the University of Virginia School of Medicine. He says his discovery changes that. The paper was published June 1 in *Nature*.

The discovery was a complete surprise to Louveau and his colleagues. While researching immune cells in the meninges, Louveau dissected entire mouse meninges. If he had cut the meninges, he believes he would never have found the lymphatic vessels. As it was, on imaging Louveau saw “immune cells aligning to a vascular structure that was not part of the cardiovascular system. We realized that the vessels that we saw were indeed lymphatic vessels.” He believes that this basic physiological discovery had gone unnoticed to this point because of the unusual location of the lymphatic vessels.

Craig Moore, a neuroscience researcher at Memorial University of Newfoundland, agrees that this is “the most convincing evidence that [lymphatic] vessels are present in the mammalian brain.” For the past decade, researchers have known that there is some type of “glymphatic” system involving glial cells that drains harmful molecules from the brain, Moore explains. “This paper provides compelling evidence for how this glymphatic system actually works.”

Researchers have known that inflammation occurs in the brain, causing cells to respond by releasing cytokines and other soluble proteins that can damage the brain. “So there obviously has to be



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Researchers have identified meningeal lymphatic vessels (red) around the meningeal blood vasculature (green).

a mechanism to drain these products so they are eliminated from the brain,” says Moore. The question was how.

This question is a critical one in neurodegenerative diseases. Moore says that in MS, for example, researchers have been looking at meningeal inflammation that leads to the demyelination of nerves. “Maybe in MS the glymphatic system is not functioning and these [products of inflammation] are not draining,” he explains. He says there is a current debate over whether the harmful molecules that fail to drain are creating “follicle-like structures” thought to affect the brains of patients with MS.

Louveau says his team believes the discovery will open new avenues not only for understanding the causes of neurological diseases but also for novel therapies. “Basically we know that there is a lymphatic system, and this might change how we see those neurological diseases.”

Moore agrees. “In neurodegenerative

diseases such as ALS and Huntington’s, you need a functioning glymphatic system to remove those molecules from the brain.” He believes creating drugs to restore the functioning of this system would help, regardless of the cause of the disease.

Although this study was in mice — the small brain size helped with visualizing the vessels — researchers believe it is a feature of all mammal brains. Louveau’s team is now “actively tracing those structures in humans” using recent cadavers. Moore also says work remains to be done to confirm the finding in the human nervous system. He plans to try to replicate the finding in his own work.

He says that the discovery will influence his research, making him more aware of lymphatic vessels while dissecting the delicate structures of the meninges. — Carolyn Brown, Ottawa, Ont.

CMAJ 2015. DOI:10.1503/cmaj.109-5100