Brain lesions associated with memory loss in multiple sclerosis linked to common brain circuit

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Between 30% and 50% of people living with multiple sclerosis (MS) will experience memory problems, but the cause is uncertain. Brain lesions
are the hallmark imaging sign used to diagnose MS and are often associated with memory dysfunction. However, increased MS brain lesions are not specific to memory problems, and are also associated with fatigue, walking difficulty and other common MS symptoms. Previous studies that attempted to align the anatomy of lesions associated with memory problems in MS led to conflicting results.

Researchers from Brigham and Women's Hospital have conducted a study to figure out which MS lesion locations are associated with memory issues. The team, led by Isaiah Kletenik, MD, analyzed imaging and cognitive data from 431 people with MS enrolled in the Comprehensive Longitudinal Investigation of MS at Brigham and Women's Hospital, or CLIMB study. Researchers mapped white matter lesion locations from each person and tested associations between memory dysfunction and a memory circuit previously derived from strokes causing memory problems.

They found that MS lesions that were associated with memory problems intersected with this memory circuit centered on the hippocampus. The researchers also analyzed the MS lesion locations compared to large functional and structural brain atlases to identify unique MS memory circuits.

The study is published in the Journal of Neurology.

"In many neurologic diseases, we know what brain function will be disrupted based on the location of lesions, but in MS, the lesions are widespread making localization challenging," Kletenik said. "By applying a circuit-based approach, we show that lesions associated with MS memory dysfunction connect to a memory circuit."

The team included researchers from the Brigham MS Center and from the Center for Brain Circuit Therapeutics led by Michael D. Fox, MD,
Ph.D. Rohit Bakshi, MD, Bonnie Glanz, Ph.D., Charles Guttmann, MD, and Tanuja Chitnis, MD, collected neuroimaging and behavioral data on people with MS as part of large, ongoing studies at the Brigham MS Center. Dr. Bakshi and Dr. Guttmann developed an imaging pipeline to automatically segment MS lesions and Dr. Glanz worked with MS Center staff to perform cognitive testing for this study.

**More information:** Isaiah Kletenik et al, Multiple sclerosis lesions that impair memory map to a connected memory circuit, *Journal of Neurology* (2023). DOI: 10.1007/s00415-023-11907-8

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