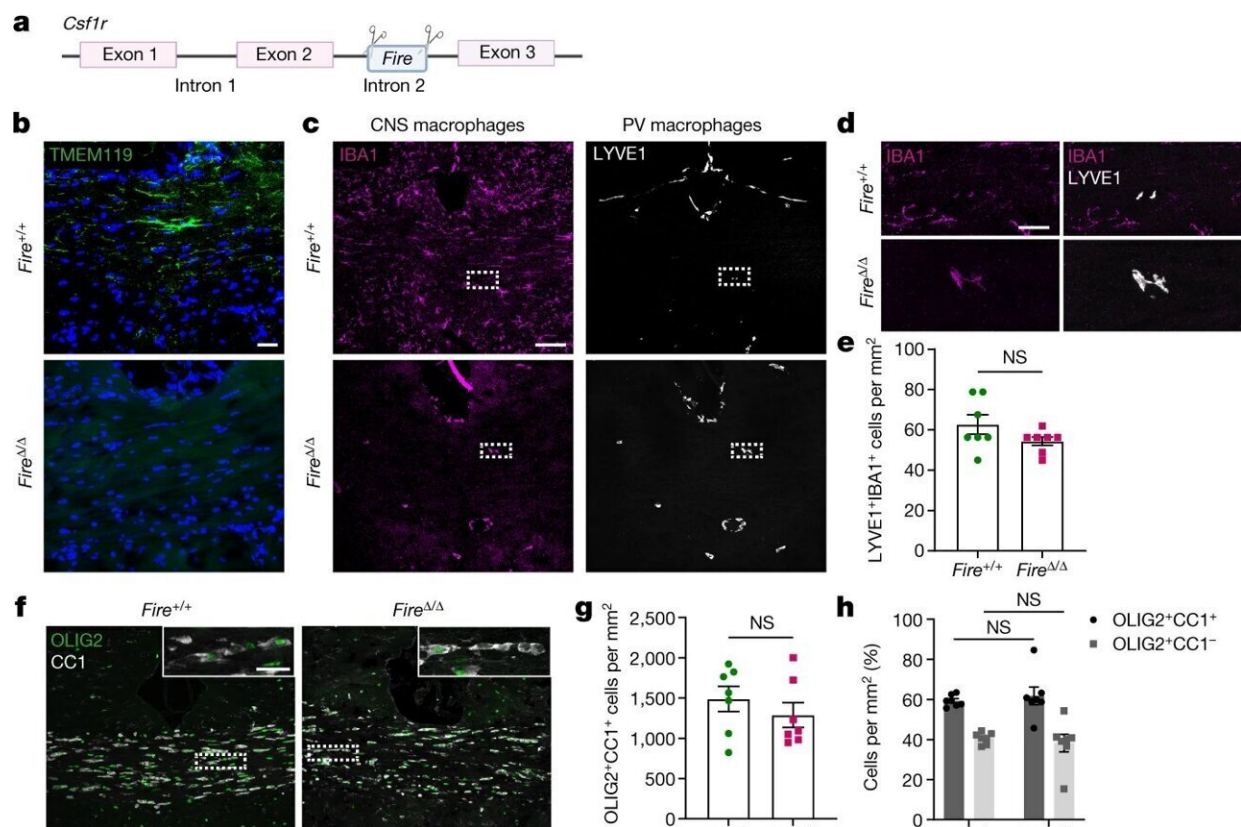


Immune cells help protect brain health and cognition, finds study

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Microglia are not required for oligodendrocyte maturation and myelination. **a**, *Fire*^{Δ/Δ} mice were generated using CRISPR9–Cas9 deletion of the *Fire* super-enhancer located in intron 2 of *Csf1r*. **b**, Images of microglia (TMEM119⁺; green) in corpus callosum samples from *Fire*^{+/+} and *Fire*^{Δ/Δ} mice at 1 month of age, counterstained with Hoechst (blue). **c**, Images of CNS macrophages (IBA1⁺; magenta) and perivascular (PV) macrophages (LYVE1⁺; white) in *Fire*^{+/+} and *Fire*^{Δ/Δ} mice. **d**, Magnified images from **c** of IBA1⁺LYVE1⁺ PV macrophages in *Fire*^{+/+} and *Fire*^{Δ/Δ} mice. **e**, Mean LYVE1⁺IBA1⁺ cells per mm² ± s.e.m. in *Fire*^{+/+}

and *Fire*^{ΔΔ} mice. *n* = 7 mice per group. *P* = 0.1411, two-tailed unpaired Student's *t*-test. **f**, Images of mature oligodendrocytes expressing both OLIG2 (green) and CC1 (white) in *Fire*^{+/+} and *Fire*^{ΔΔ} mice. Inset shows magnified view. **g**, Mean OLIG2⁺CC1⁺ cells per mm² ± s.e.m. in *Fire*^{+/+} and *Fire*^{ΔΔ} mice. *n* = 7 mice per group. *P* = 0.1990, two-tailed unpaired Student's *t*-test. **h**, Mean proportion of cells of the oligodendrocyte lineage (OLIG2⁺), which are mature (CC1⁺; black) or immature (CC1⁻; gray) (±s.e.m.). *n* = 7 mice per group. CC1⁺, *P* = 0.9472; CC1⁻, *P* = 0.9472; one-way analysis of variance (ANOVA) with Tukey's multiple comparisons test. **i**, Images of corpus callosum from *Fire*^{+/+} and *Fire*^{ΔΔ} mice stained for the myelin proteins MAG (green) and MBP (magenta) (left and middle) and imaged by electron microscopy (right). **j**, Mean number of myelinated axons per mm² ± s.e.m. in corpus callosum from *Fire*^{+/+} and *Fire*^{ΔΔ} mice. *n* = 3 *Fire*^{+/+} mice and 4 *Fire*^{ΔΔ} mice. *P* = 0.5216, two-tailed unpaired Student's *t*-test. **k**, Mean number of myelinated axons in corpus callosum from *Fire*^{+/+} and *Fire*^{ΔΔ} mice per axon diameter. *n* = 3 *Fire*^{+/+} mice and 4 *Fire*^{ΔΔ} mice. *P* = 0.9139, two-way ANOVA with Sidak's multiple comparisons test. Scale bars, 25 μm (**b,d,i** (left and middle)), 75 μm (**c,f**) and 1 μm (**i** (right))). Credit: *Nature* (2022). DOI: 10.1038/s41586-022-05534-y

Scientists have discovered that immune cells, known as microglia, help maintain the health of myelin—the insulating layer that forms around nerve cells—which is important for nerve cells in the brain and spinal cord to function optimally.

Changes in the structure of myelin and damage to myelin are considered to contribute to the early stages of dementia, but the mechanisms underlying these changes are, until now, poorly understood.

The findings can be used to better understand what goes wrong in the brain in dementia and pave the way for potential future treatments, experts say.

In mice without [microglia](#), scientists from the UK Dementia Research

Institute at the University of Edinburgh observed the same changes to myelin that are seen with aging and in neurodegenerative disease, which are associated with cognitive decline.

The same changes are present in a [rare genetic disorder](#) called ALS, which is characterized by early-onset dementia. In ALS a decrease in microglia occurs specifically in areas of the brain that have a high level of myelin.

Myelin damage

The team discovered that a signaling molecule released by microglia called TGF- β is important to keep myelin in a healthy state.

They plan to build on this work by understanding how microglia and TGF- β are altered in [neurodegenerative diseases](#) where myelin damage and [cognitive decline](#) occur, like multiple sclerosis and Alzheimer's disease.

The findings have been published in *Nature*.

"Our data revealed a surprising protective role for microglia in maintaining the health of myelin. If you have less microglia, the myelin falls apart, and cognition suffers. Our work also suggests that microglia may lose this protective function with aging and in dementia, potentially kickstarting myelin damage and a decline in cognitive function," says Professor Veronique Miron, Lead researcher from UK Dementia Research Institute at the University of Edinburgh.

"We lack therapies that can effectively slow or stop the progression of dementia. We do know, however, that healthy myelin is needed for healthy cognition, and that changes in myelin are associated with the early stages of cognitive impairment. Better understanding of what keeps

myelin healthy, and how myelin is damaged, will bring us one step closer to developing an effective therapy to stop dementia in its tracks at an early stage," says Dr. Niamh McNamara, First author and researcher at the University of Edinburgh

More information: Veronique Miron, Microglia regulate central nervous system myelin growth and integrity, *Nature* (2022). [DOI: 10.1038/s41586-022-05534-y](https://doi.org/10.1038/s41586-022-05534-y).
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Provided by University of Edinburgh

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