Researchers report novel complementary effects of estrogen treatment in multiple sclerosis

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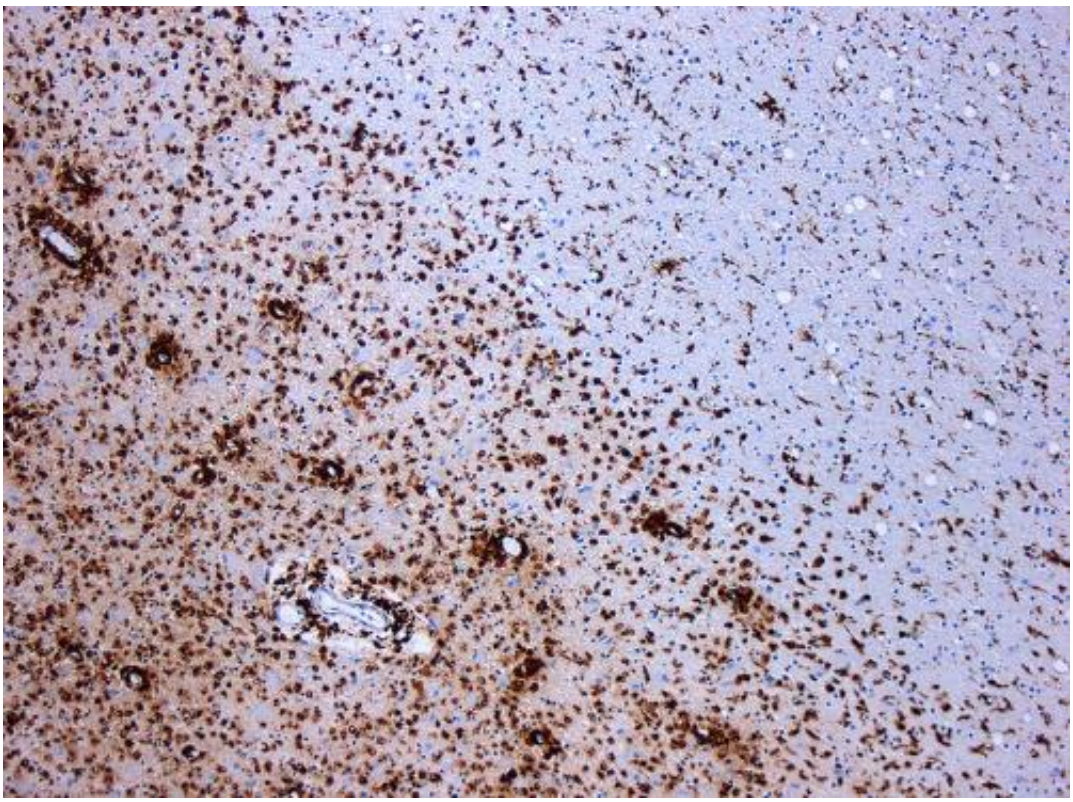

Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: CC BY-SA 3.0 Marvin 101/Wikipedia

A study by UCLA researchers reveals the cellular basis for how the

hormone estrogen protects against damage to the central nervous system in people with multiple sclerosis (MS). The researchers found that estrogen treatment exerts positive effects on two types of cells during disease —immune cells in the brain and also cells called oligodendrocytes. Complementary actions on these two types provide protection from disease.

Multiple sclerosis is a chronic autoimmune, neurodegenerative disease marked by visual impairment, weakness and sensory loss, as well as cognitive decline. These symptoms emerge when inflammatory immune cells destroy the myelin sheath that surrounds nerve processes called axons. Loss of that protective insulation disrupts electrical communication between nerve cells.

The third trimester of pregnancy has been previously shown to reduce relapse rates by approximately 70 percent as compared to before pregnancy, and other studies have shown benefit over the long term due to multiple pregnancies. An estrogen unique to pregnancy that is made by the fetus and placenta has been proposed by Dr. Rhonda Voskuhl and colleagues to mediate this pregnancy protection in both the MS mouse model as well as in two successfully completed clinical trials of estriol treatment in MS patients.

How that happens has remained a critical question. Voskuhl, who led the latest study, reported mouse studies showing that estrogen protected the brain from damage by activating a protein called estrogen receptor beta (ERb). Her new research identifies which cells within the brain are mediating this protective effect.

The researchers first genetically eliminated ERb in either immune cells of the brain or in oligodendrocytes, the cells that make the myelin sheath, as a way of making cells unresponsive to estrogen during the MS like disease in mice. They then treated mice without or with ERb in

these cells to ask if disease protection was lost or not. Loss of protection during treatment meant that the treatment was acting on the cell that had the receptor removed. Results showed that the estrogen-like treatment was acting on both immune cells of the brain as well as on oligodendrocytes, together resulting in repair of myelin and less disability.

Drug developers often optimize therapies by targeting only one single cell type. By contrast, this study confirms that this estrogen-like compound can combat MS via complementary effects on two distinct cell types. Voskuhl and other UCLA researchers are in fact now developing a next-generation estrogen-like compound with robust biochemical effects on oligodendrocytes and immune cells in the brain.

The study was published online in *Brain* on Dec. 8. It will appear in the January print issue.

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