

Remyelinating drug could improve vision in patients with multiple sclerosis

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Maria Sekyi (left), the first author of the research paper, is seen here with Seema Tiwari-Woodruff, the study's lead author, in a photo dated Sept. 13, 2019. Credit: Tiwari-Woodruff lab, UC Riverside.

A team led by a biomedical scientist at the University of California, Riverside, reports a drug—an estrogen receptor ligand called indazole

chloride (IndCl)—has the potential to improve vision in patients with multiple sclerosis, or MS.

The study, performed on mice induced with a model of MS and the first to investigate IndCl's effect on the pathology and function of the complete afferent visual pathway, is published in *Brain Pathology*. The afferent visual pathway includes the eyes, optic nerve, and all brain structures responsible for receiving, transmitting, and processing [visual information](#).

In MS, a disease in which the immune system "demyelinates" or eats away at the protective covering of nerves, the initial period of inflammation and demyelination often damages the optic nerve and other parts of the visual system first. As a result, approximately 50% of patients with MS experience [optic neuritis](#)—inflammatory demyelination of the optic nerve—prior to showing initial symptoms. Almost all MS patients have impaired vision at some point during disease progression. Symptoms can include eye pain, blurred vision, and progressive vision loss that can lead to blindness, among other [visual impairments](#).

The optic nerve, a heavily myelinated bundle of nerves located at the back of the eye, transfers visual information from the retina to the vision centers of the brain through electrical impulses. Myelin acts as an insulating substance that speeds the transmission of these electrical impulses. Partial myelin loss slows transmission of visual information; severe myelin loss may stop the signal altogether.

The researchers used IndCl to assess its impact on demyelinating visual pathway axons. The treatment induced remyelination and mitigated some damage to the axons that resulted in partial functional improvement in vision.

"IndCl has been previously shown in mice to reduce motor disability, increase myelination, and neuroprotection in the spinal cord and corpus callosum," said Seema Tiwari-Woodruff, a professor of biomedical sciences at the UC Riverside School of Medicine and the study's lead author. "Its effects in the visual system, however, were not evaluated until now. Our study shows the [optic nerve](#) and optic tract, which undergo significant inflammation, demyelination, and axonal damage, are able to restore some function with IndCl treatment with successful attenuation in inflammation and an increase in remyelination."

The visual pathway in mice is similar to that in humans. The mouse brain is, therefore, an excellent model for scientists to study vision impairment. In the lab, Tiwari-Woodruff and her research group first induced the mouse model of MS. They let the disease progress for about 60 days and when the disease reached a peak between 15 and 21 days, they administered IndCl to half the mice. At the end of the experiment, they performed [functional assay](#) to measure the visual electrical signal; and [immunohistochemistry](#) to examine the visual pathway. The mice that received the drug showed improvement in myelination, with visual function improving by about 50%.

For Tiwari-Woodruff, the next question is how IndCl treatment induces functional remyelination in the visual pathway. Her lab, in collaboration with the lab of co-author John A. Katzenellenbogen at the University of Illinois at Urbana-Champaign, is investigating new drugs that are analogues of IndCl.

"Measuring visual function and recovery in the presence of novel therapies can be used to screen more effective therapies that will protect axons, stimulate axon remyelination, and prevent ongoing axon damage," Tiwari-Woodruff said.

Currently approved MS drugs reduce inflammation but do not prevent

neurodegeneration or initiate remyelination. Further, they only partially prevent the onset of permanent disability in patients with MS.

"We treated the MS mice with IndCl at peak disease," Tiwari-Woodruff said. "If the brain is highly diseased, some of the axons that could potentially restore visual function are too damaged and will not recover. There's a point of no return. Our paper stresses that to acquire vision improvement, treatment must start early. Early treatment can recover 75%-80% of the original function."

Tiwari-Woodruff stressed that although additional studies are required, the new findings show the dynamics of visual pathway dysfunction and disability in MS mice, along with the importance of early treatment to mitigate axon damage.

"There is a strong and urgent need to find a therapeutic candidate that restores neurological function in patients with MS," Tiwari-Woodruff said. "Therapeutics must target remyelination and prevent further axonal degeneration and neuronal loss. The good estrogens, which have neuroprotective and immunomodulatory benefits, could be candidates for MS treatment."

More information: Maria T. Sekyi et al, Alleviation of extensive visual pathway dysfunction by a remyelinating drug in a chronic mouse model of multiple sclerosis, *Brain Pathology* (2020). [DOI: 10.1111/bpa.12930](https://doi.org/10.1111/bpa.12930)

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