New study reshapes understanding of how the brain recovers from injury

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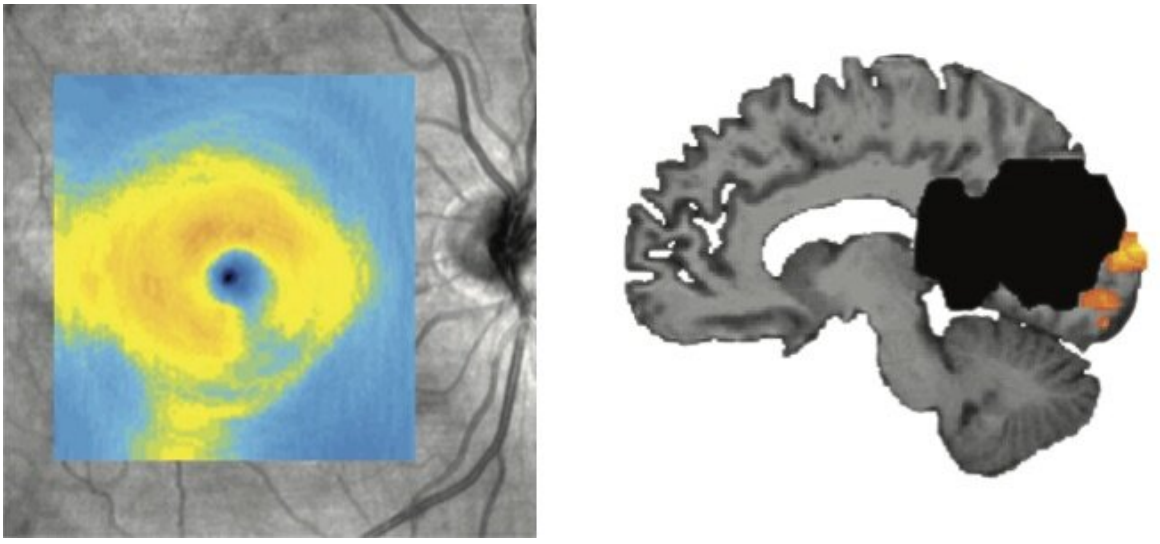

The left image shows degeneration that typically occurs in the eye (lower right corner) after a patient has a stroke in the visual processing area of the brain. The area of degeneration corresponds to the location of blind areas of the patient's visual field. Carnegie Mellon and University of Rochester researchers found the eye is less likely to degenerate when the brain continues to respond to visual stimuli despite the patient's blindness from the stroke. The right image shows lesion in black and visual cortex activity to stimuli presented in blind areas of the patient's visual field in orange. Credit: Schneider et al.

Each year, approximately 265,000 Americans have a stroke that causes visual impairment. New research, which appears in the journal

Proceedings of the Royal Society B, sheds light on how the damage in the brain caused by a stroke can lead to permanent vision impairment. The findings could provide researchers with a blueprint to better identify which areas of vision are recoverable, facilitating the development of more effective interventions to encourage vision recovery.

"This study breaks new ground by describing the cascade of processes that occur after a stroke in the visual center of the brain and how this ultimately leads to changes in the retina," said senior study author Brad Mahon, an associate professor at Carnegie Mellon University and the University of Rochester. "By more precisely understanding which connections between the eye and brain remain intact after a stroke, we can begin to explore therapies that encourage neuroplasticity with the ultimate goal of restoring more vision in more patients."

When a stroke occurs in the primary visual cortex, the neurons responsible for processing vision can be damaged. Depending upon the extent of the damage, this can result in blind areas in the field of vision. While some patients spontaneously recover vision over time, for most the loss is permanent. A long-known consequence of damage to neurons in this area of the brain is the progressive atrophy of cells in the eyes, called retinal ganglion cells.

"While the eye is not injured in the stroke, cells in the retina that send projections to parts of the brain that are damaged will degenerate over time," Mahon said. "Once this occurs, it becomes more and more unlikely for vision to recover at that location."

The new research sought to understand the mechanisms of vision loss after stroke and whether it was possible to identify areas in the field of vision that could be recovered. The study involved 15 patients treated at Strong Memorial and Rochester General hospitals for a stroke that affected the primary visual processing area of the brain. The participants

took vision tests, underwent scans in an MRI to identify areas of brain activity and were administered a test that evaluated the integrity of cells in their retina.

The team found that the survival of the retinal ganglion cells depended upon whether or not the primary visual area of the brain to which they are connected remained active. Eye cells that were connected to areas of visual cortex that were no longer active would atrophy and degenerate, leading to permanent visual impairment.

However, the researchers observed that some cells in the eye remained healthy, even though the patient could not see at the corresponding field of vision. This finding suggests that these eye cells remain connected to unscathed neurons in the visual cortex and that visual information was making its way from the eyes to the visual cortex, even though this information was not being interpreted by the brain in a manner that allowed sight.

"The integration of a number of cortical regions of the brain is necessary in order for visual information to be translated into a coherent visual representation of the world," said study co-author Dr. Bogachan Sahin, an assistant professor in the University of Rochester Medical Center (URMC) Department of Neurology. "And while the stroke may have disrupted the transmission of information from the visual center of the brain to higher order areas, these findings suggest that when the primary visual processing center of the brain remains intact and active, clinical approaches that harness the brain's plasticity could lead to vision recovery."

The research has formed the basis of a new clinical trial for stroke patients with vision loss that is now under way at URMC and lead by Sahin. The study involves a class of drugs called selective serotonin reuptake inhibitors, the most common of which is the antidepressant

Prozac, which are known to enhance neuroplasticity—the brain's ability to rewire itself and form new connections to restore function after damage. The hypothesis is that the drug will help restore vision by fostering the development of new connections between areas of the brain necessary for interpreting signals from the healthy eye cells.

The study also suggests new clinical approaches to maximize the potential for recovery by more effectively targeting blind regions in the field of vision. URMC researchers Krystel Huxlin and Dr. James V. Aquavella have developed a visual training regime that has been shown to help with vision recovery after stroke and the new study could help refine how this technology is employed.

"These findings suggest a treatment protocol that involves a visual field test and an eye exam to identify discordance between the visual deficit and retinal ganglion cell degeneration," said Colleen Schneider, an M.D./Ph.D. student at the University of Rochester School of Medicine and Dentistry and the first author of the study. "This could identify areas of vision with intact connections between the eyes and the brain and this information could be used to target visual retraining therapies to regions of the blind field of vision that are most likely to recover."

Data from this study is openly available in KiltHub, CMU's comprehensive institutional repository hosted within figshare. In the future, it will be incorporated into The Open Brain Project, a new, digital platform for exploration of the human brain. Ana Van Gulick, research liaison for psychology and brain sciences and program director for Open Science at Carnegie Mellon University Libraries, is a key contributor to this joint effort of CMU and the University of Rochester.

"The field of neuroscience is currently undergoing a dramatic shift toward open science that will encourage new collaborations and methods of research inspired by data science," Van Gulick said. "A cornerstone

of this is providing open access to datasets in a standard format so that they can be aggregated and reused to extend scientific discovery. The data currently available in KiltHub and the larger collection that will later be discoverable through The Open Brain Project will provide a rich open access resource for education and research in neuroscience."

This study also is part of a larger research program being carried out by the Translational Brain Mapping Program at the University of Rochester Medical Center. Mahon and Sahin were recently awarded a $1.7 million grant from National Eye Institute to continue their investigations into vision loss after stroke. The funding will support a multi-institution research effort that includes CMU, URMC, Rochester Regional Health and the University of Pittsburgh Medical Center.

Additional co-authors of the study include Emily Prentiss, Ania Busza and Zoe Williams with URMC and Kelly Matmati and Nabil Matmati with Rochester Regional Health. The study was supported with funding from the National Institute of Neurological Disorders and Stroke, the National Eye Institute, the Schmitt Program on Integrative Brain Research and Research to Prevent Blindness.

More information: Colleen L. Schneider et al, Survival of retinal ganglion cells after damage to the occipital lobe in humans is activity dependent, *Proceedings of the Royal Society B: Biological Sciences* (2019). DOI: 10.1098/rspb.2018.2733

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