Can your brain control how it loses control?

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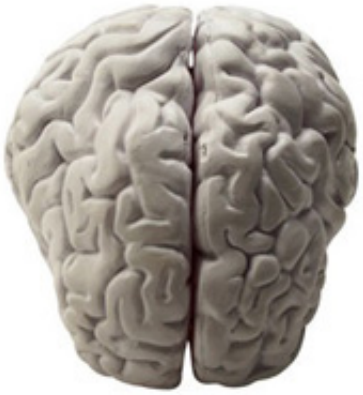

A new study may have unlocked understanding of a mysterious part of the brain—with implications for neurodegenerative conditions such as Alzheimer's. The results, published in *Translational Vision Science & Technology* (*TVST*), open up new areas of research in the pursuit of neuroprotective therapies.

Glaucoma is a neurodegenerative disease where patients lose seemingly random patches of vision in each eye. This random pattern of vision loss is in stark contrast to loss from a brain tumor or stroke, which causes both eyes to develop blind spots in the same location. Scientists have long thought that glaucoma's progression is independent of - or uncontrolled by - the brain.

Last year, researchers found evidence that the progression of glaucoma is not random and that the brain may be involved after all. Specifically, they found patients with moderate to severe glaucoma maintained vision in one eye where it was lost in the other—like two puzzle pieces fitting together (a "Jigsaw Effect"). "This suggests some communication between the eyes must be going on and that can only happen in the brain," explains the study's lead author, William Eric Sponsel, MD, of the University of Texas at San Antonio, Department of Biomedical Engineering.

In the latest TVST paper, Refined Frequency Doubling Perimetry Analysis Reaffirms Central Nervous System Control of Chronic Glaucomatous Neurodegeneration, Sponsel and his research team found that the Jigsaw Effect begins at the earliest stages of glaucoma and discovered clues as to which part of the brain is responsible for optimizing vision in the face of glaucoma's slow destruction of sight.

However, these findings, which challenge longstanding assumptions about glaucoma, have been met with skepticism. Other glaucoma experts challenged the results in a letter to the TVST editor. "If the brain controls the distribution of vision loss in glaucoma, then a patient's vision with their two eyes should be better than if you simply 'mix and match' the vision of right and left eyes from different patients," explained letter co-author Paul Artes, PhD, of Plymouth University, Department of Eye and Visual Sciences. Along with co-author Jonathan Denniss, PhD, University of Nottingham, Visual Neuroscience Group, their letter analyzed a new cohort of glaucoma patients in which "that's essentially what we did. And we did not find any visual advantage in a patient's own eyes versus the combined vision in eyes from different patients; indeed we found the opposite effect."

Sponsel and co-authors responded to the letter to the editor with their own. "Our analysis of the data [Artes and Denniss] introduced

demonstrated conclusively that the 'Jigsaw Effect' was indisputably present in patients we had never even seen. Moreover, we were able to confirm that the alternative analytical method they proposed could not reliably detect very obvious computer-generated complementary visual field pairs," like a left and right eye that could only see opposite halves of their normal field of vision, says Sponsel. "The problem with their approach was their assumption that a single brain could somehow combine information from the eyes of different human beings. We studied individual people with naturally paired eyeballs connected to a single brain."

The key to finding where the brain coordinates vision loss was found in small-scale, arc-shaped patterns of vision displayed by patients. Co-author Ted Maddess, PhD, of the Australian National University, Center of Excellence in Vision Science, explains that these patterns mimic structures found at the very back of the brain, known as ocular dominance columns. While their function is not completely understood, what is known is that some ocular dominance columns are associated with the left eye and other columns with the right.

The new paper suggests that the narrow spaces between ocular dominance columns associated with the left and right eye are where the brain coordinates each eye's working field of vision. Depending on what the brain needs, those narrow spaces can function with either eye "much like a bilingual person living near the border of two countries," explains Sponsel.

The progression of Alzheimer's and Parkinson's diseases, which have neurodegenerative biology similar to glaucoma, may also be actively mediated by the brain. "Our work has illustrated that the brain will not let us lose control of the same function on both sides of the brain if that can be avoided. It seems likely that the same kind of protective mechanism will be at work with other neurodegenerative disorders," he

says.

The investigative team believes that if the brain regulates neurodegeneration - that if the brain controls how it loses control - then researchers will now be able to look into largely unexplored regulatory processes for opportunities to slow or stop the progression of these diseases.

"We've opened up this beautiful new world; there is so much to discover here," says Sponsel.

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