Why does visual field loss follow one pattern and not another? Why is there a temporal crescent in the visual field to be lost? To answer these questions, we could look at the anatomy of the optic nerve and the configuration of nerve fibers and how they are damaged by chronic pressure elevation. But this leads to deeper questions such as why the optic nerve is structured as it is. Ultimately, we might wonder whether there is a survival benefit to the sequence of loss. Although there are many exceptions, field loss in moderate glaucoma seems to more often occur peripherally rather than centrally and superiorly rather than inferiorly. One could argue that this maximizes our ability to function despite glaucoma damage. In fact, I have been very impressed over the years that patients frequently are unaware of visual field loss—even when it is quite extensive.

In this month’s “Glaucoma editor’s corner of the world,” William E. Sponsel, MD, discusses a study that looked at the pattern of visual loss in patients with very advanced damage. He found that non-overlapping areas were preferentially preserved in each eye. He hypothesizes that this allows us to maintain maximum visual function even when the vast majority of optic nerve capacity has been destroyed. And indeed, my experience has been that many patients with advanced disease—while clearly aware that they have profound visual loss, do continue to have surprising functional ability. The pattern of visual loss in advanced glaucoma is an important area of research, and Dr. Sponsel thinks this may have implications for other neurodegenerative diseases.

**Study shows that the brain controls cell loss in glaucomatous neurodegeneration to preserve the binocular visual field**

Through a remarkable refined data analysis of visual fields from patients with bilaterally stable/severe glaucoma, a study published in the May 2014 issue of *Translational Vision Science and Technology* provides evidence that the brain controls and coordinates ganglion cell loss between both eyes in order to preserve the best possible binocular visual field.

“What we’ve discovered here is that the brain and the 2 eyes are working together as a unit,” said William E. Sponsel, MD, glaucoma specialist and professor of biomedical engineering, University of Texas at San Antonio, the study’s lead author.

While visual field loss in glaucoma seems haphazard and random when the eyes are analyzed separately, Dr. Sponsel’s team found that when the 2 visual fields are superimposed, they are complementary—areas of permanent vision loss in 1 eye correspond to areas that are seen well in the other eye. The 2 fields fit together like a jigsaw puzzle, so that patients have much better vision with both eyes than could possibly arise by chance if ganglion cell loss was progressing independently in each eye.

“The brain/eye complex is doing wonderful things to keep people mobile and in surprisingly good functional condition in spite of severe axonal loss, by resisting loss of vision in the same area of the visual field in both eyes at once,” Dr. Sponsel said.

**The path to understanding**

The jigsaw phenomenon has been there all along, but several obstacles have prevented clinicians from recognizing it, Dr. Sponsel said. The effect is not readily seen in patients with mild to moderate disease—it only becomes clear once a person has lost 70% to 80% of the ganglion cells and the Humphrey visual field printouts have large areas of black.

Next, IOP must be under control and injured axons that are still alive allowed to recover, outcomes Dr. Sponsel achieved surgically with non-penetrating deep sclerectomy (NPDS) procedures. Postoperatively, patients’ IOPs were low and stable, cell function returned, and patient sensitivity to light increased, allowing the reversible gray areas of the visual field printout to become white again. The contrast between white and black areas finally revealed the complementarity between each eye’s visual field—and the brain’s role in controlling it.

After qualitatively observing the effect in post-NPDS patients, Dr. Sponsel’s team performed a sophisticated statistical analysis of the visual fields of 47 patients with bilaterally severe glaucoma. They found that the tendency to create complementary visual fields—the preservation of binocular vision—was so great that the probability that it was due to chance was less than 0.000000001%. Passive anatomic symmetry factors did not contribute to the effect, indicating that the CNS must be coordinating the bilateral compensatory process.

“The chances of this happening by coincidence are so infinitesimally small, it’s effective proof that the brain must be in control of this process,” Dr. Sponsel concluded. “The fact is, given the extensive level of eye/brain neural integration that is already well known, there’s no way the brain should let the same functional areas be lost simultaneously if it can possibly avoid it.”

**The brain in control**

According to Dr. Sponsel, the evidence for central nervous system control over vision loss in glaucoma has been there all the time—but it has been curiously overlooked. If the brain was not involved and ganglion cell loss was purely the result of decreased blood supply, central vision would be the last thing to go in glaucoma—but it is not.

The final area of vision lost is the temporal crescent, the monocular visual field for which the fellow eye cannot compensate.

That is the most distal, nasal retina, farthest away from the blood supply, with some of the most diffuse wiring in the entire eyeball,” Dr. Sponsel said. “So how could that possibly happen by chance?”

The discovery of the jigsaw effect is nothing short of remarkable, not only for its impact on ophthalmology, but for neurobiology as well. The question is, if the brain preserves the best bilateral function during degeneration of the retina, does it do so for other neurodegenerative diseases as well?

The mechanisms of progression in open-angle glaucoma are surprisingly similar to those of Alzheimer’s disease, so that conclusion is a distinct possibility.

“Both age-related disorders progress bilaterally, involving both eyes and both cerebral hemispheres, respectively, and each disorder exhibits focally asymmetric neurodegeneration,” the study authors wrote.

Testing that hypothesis in other brain disorders would be a challenge, however, because an Alzheimer’s patient would not survive long enough to reach the level of neurodegeneration in the cerebral cortex that is needed to readily observe the jigsaw effect in the paired retinas, where structure and function coincide precisely in exquisite 2-dimensional bilaterally symmetric arrays.

Despite the obstacles, Dr. Sponsel remains excited about the possibilities of future work. His next step is to correlate the pathological evidence of the jigsaw effect with visual field results. Areas of ganglion cell loss, observed by thinning of the retinal nerve fiber layer seen on OCT, should overlap with the areas of visual field loss seen on the Humphrey test.

“This is an amazing thing to have the pleasure of discovering,” he said. “It’s one of these discoveries that you just pinch yourself that you’re so lucky to be alive to have anything to do with it. I am so grateful to my collaborators, our skilled clinical team, and all the patients who trusted us with their care.” EW

**Editors’ note:** Dr. Sponsel has no financial interests related to his comments.

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