

Access this article online
Quick Response Code:

Website: www.e-tjo.org
DOI: 10.4103/tjo.tjo_74_20

# Homonymous thinning on macular optical coherence tomography indicating retrograde trans-synaptic degeneration from occipital infarctions

Benjamin I. Meyer<sup>1</sup>, Benson S. Chen<sup>1</sup>, Valérie Biousse<sup>1,2</sup>, Nancy J. Newman<sup>1,2,3\*</sup>

## Abstract:

Inner retinal thinning on optical coherence tomography (OCT) occurring through retrograde trans-synaptic degeneration is an increasingly recognized phenomenon, even in acquired retro-chiasmal brain lesions. We describe a man with stable visual field defects from multiple bilateral posterior circulation infarctions, who had ganglion cell complex (GCC) thinning on macular OCT that corresponded precisely with his visual field defects. In contrast to previous reports indicating that peripapillary retinal nerve fiber layer (RNFL) changes are important in detecting this phenomenon, the peripapillary RNFL thickness and the optic disc appearance of our patient were relatively unaffected. Our case contributes to the growing body of evidence that retrograde trans-synaptic degeneration can manifest as isolated macular OCT findings.

## Keywords:

Infarction, macular ganglion cell complex, optical coherence tomography, trans-synaptic retrograde degeneration, visual field defects

## Introduction

The widespread implementation of optical coherence tomography (OCT) has fundamentally transformed the way that many ophthalmic diseases are diagnosed, characterized, and managed. This is also true for neuro-ophthalmologic conditions, in which OCT can detect inner retinal and peripapillary optic nerve changes that were previously too subtle to identify or quantify clinically.<sup>[1]</sup> One such process that has been long-debated is retrograde trans-synaptic degeneration, whereupon lesions in the brain manifest with changes in the retina.<sup>[2]</sup>

Classically, it has been taught that intracranial lesions involving the visual pathways anterior to the lateral geniculate nucleus (LGN) could cause retinal changes (simple retrograde

degeneration of ganglion cell axons), whereas lesions posterior to the LGN could not.<sup>[3,4]</sup> With the implementation of OCT, it has been shown that acquired lesions of the visual pathways posterior to the LGN can indeed exhibit retrograde trans-synaptic degeneration.<sup>[5]</sup> While this process is increasingly recognized, the significance of specific variables remains controversial, including the proximity of injury in relation to the LGN, the age of the patient, the chronicity of the lesion, and the different ophthalmic manifestations. Reliance upon concurrent peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell complex (GCC) thinning to detect this process has been extensively reported.<sup>[5-8]</sup> However, there are relatively few reports of isolated OCT macular changes, with sparing of the peripapillary RNFL and optic disc appearance, characterizing this process.<sup>[9-11]</sup>

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Meyer BI, Chen BS, Biousse V, Newman NJ. Homonymous thinning on macular optical coherence tomography indicating retrograde trans-synaptic degeneration from occipital infarctions. Taiwan J Ophthalmol 2021;11:89-92.

Departments of  
<sup>1</sup>Ophthalmology,  
<sup>2</sup>Neurology and  
<sup>3</sup>Neurological Surgery,  
Emory University School  
of Medicine, Atlanta,  
Georgia, USA

### \*Address for correspondence:

Dr. Nancy J. Newman,  
1365B Clifton Road, NE,  
Atlanta, Georgia 30322,  
USA.

E-mail: ophthn@emory.edu

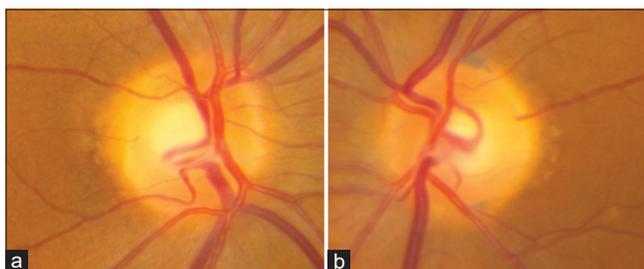
Submission: 31-08-2020  
Accepted: 03-10-2020  
Published: 23-01-2021

We describe an adult patient with acquired post-geniculate intracranial visual pathway lesions whose retrograde trans-synaptic degeneration manifested with primarily macular GCC thinning. The pattern of macular changes corresponded identically to his visual field defects. His peripapillary RNFL and optic nerve appearance were relatively unaffected.

### Case Report

A 59-year-old man with a previous history of multifocal bilateral posterior circulation cerebral infarctions from paroxysmal atrial fibrillation was referred for neuro-ophthalmologic evaluation for persistent visual field deficits 3 years after his strokes. He had no past ocular history. The patient had presented with sudden vision loss to the right side in both eyes' field of vision. He also reported binocular loss of color vision and difficulty reading. Brain magnetic resonance imaging at the time revealed acute infarctions of the left posterior cerebral artery territory involving the left occipital and temporal lobes, left thalamus, and left hippocampus, as well as punctate acute infarctions involving the right medial occipital lobe. On neurological examination upon discharge, he had a right homonymous superior quadrantanopia to confrontation, alexia without agraphia, and prosopagnosia.

On evaluation 3 years later, the patient reported subjective improvement in his reading ability. Visual acuities were 20/20 in the right eye and 20/15-2 in the left eye, and color vision with Ishihara plates was 12 of 14 correct in the right eye and 13 of 14 correct in the left eye. Pupils were normal. Dilated fundus examination revealed cup-to-disc ratios of 0.3 in both eyes and normal optic nerves without visible pallor [Figure 1]. Automated perimetry demonstrated a right homonymous superior quadrantanopia and left homonymous superior paracentral scotomatous defects [Figure 2]. OCT of the peripapillary RNFL (Cirrus HD-OCT 5000, Zeiss, Oberkochen, Germany) was within normal limits except for mild inferonasal thinning in the right eye and mild inferotemporal thinning in the left eye as seen on the temporal-superior-nasal-inferior-temporal (TSNIT)



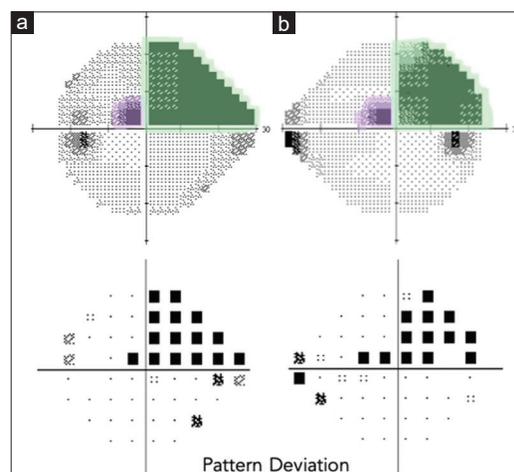
**Figure 1:** Fundus photography. Centered on the right (a) and left (b) optic nerve heads, demonstrating normal appearances without discernible pallor

graph [Figure 3]. Macular OCT showed inferior homonymous GCC thinning to the left and right of the foveae, worse to the left in both eyes, corresponding precisely with his visual field defects [Figure 4].

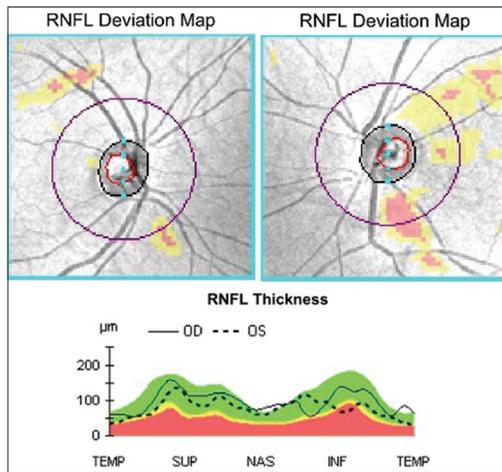
### Discussion

We present a case of a man with stable visual field defects 3 years after bilateral posterior circulation infarctions, and evidence of macular GCC thinning on OCT. The macular changes corresponded precisely with the right homonymous superior quadrantanopia and left homonymous superior paracentral scotomatous defects. Notably, his optic nerve appearances were not recognizably affected, with only borderline RNFL thinning on the TSNIT graph. This case supports the fact that acquired lesions posterior to the LGN can cause retrograde trans-synaptic degeneration with macular changes detectable on OCT.

Trans-synaptic degeneration is thought to occur from a paucity of trophic signals to neighboring axons after neuronal injury or death, which disrupts the functional network that is essential for cellular viability.<sup>[12]</sup> Anterograde (“Wallerian”) degeneration, implicating neurons upstream of an injury, has been well-studied, with evidence of retinal lesions leading to LGN atrophy.<sup>[2,4,13]</sup> In contrast, retrograde degeneration from postgeniculate lesions was previously presumed unlikely, given an additional degree of separation between the lesion involving the occipital cortex and the axons of the retinal ganglion cells in the optic tract.<sup>[4]</sup> Evidence supporting trans-synaptic retrograde degeneration in the visual pathways was first described in animal studies that demonstrated loss of the retinal ganglion cell layer on histological specimens in monkeys with simultaneous



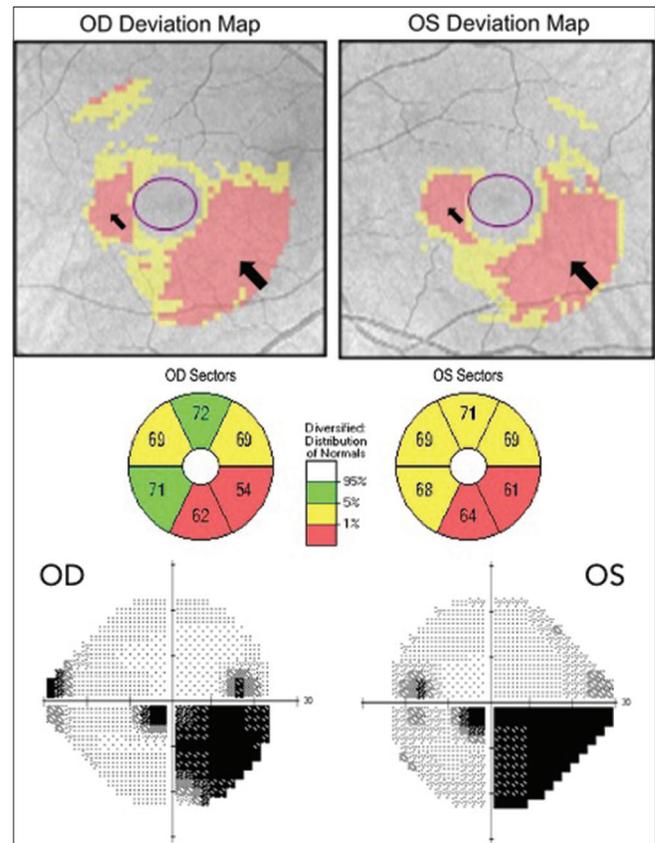
**Figure 2:** Humphrey visual field testing 24-2 SITA-FAST HVF demonstrating a right homonymous superior quadrantanopia (green) and left homonymous superior paracentral scotomatous defects (purple). These visual fields were unchanged from 6-months after stroke (not shown). Left eye (a) and right eye (b)



**Figure 3:** Optical coherence tomography (OCT, Cirrus HD-OCT 5000, Zeiss, Oberkochen, Germany) of the peripapillary retinal nerve fiber layer (RNFL) is within normal limits except for some mild inferonasal thinning in the right eye and mild inferotemporal thinning in the left eye on TSNIT graph, averaging 98  $\mu\text{m}$  in the right eye and 80  $\mu\text{m}$  in the left eye

optic chiasmal and occipital lesions.<sup>[14]</sup> Retinal hypoplasia in a pattern mirroring homonymous visual field defects was demonstrated in children with congenital retro-geniculate lesions, and histological verification of retrograde trans-synaptic degeneration of the human visual system soon followed.<sup>[15,16]</sup> However, these data were all from patients whose insults occurred in development or childhood, and it was presumed that acquired lesions in later life would not demonstrate the same retrograde degenerative process.<sup>[3]</sup> With advancing technology, pattern electroretinograms demonstrated decreased amplitudes in the hemi-retinae that topographically corresponded to acquired post-geniculate lesions, and OCT exhibited peripapillary RNFL degeneration within 1 to 2 years following a stroke.<sup>[5,6,17]</sup> Research has now shifted towards better characterizing this process and its ophthalmic manifestations.

Until recently, studies of the ophthalmic manifestations of patients with post-geniculate lesions have focused on peripapillary RNFL changes following strokes. A study of 38 patients with occipital strokes found a negative linear relationship between RNFL thickness and time elapsed since infarction, with a decelerating rate of thinning.<sup>[6]</sup> Patients whose RNFLs were closest to normal following their strokes exhibited greater visual recovery.<sup>[6]</sup> Hence, in patients without retinal changes, peripapillary RNFL thinning has been proposed as a prognostic indicator of long-term visual outcome.<sup>[7,8]</sup> However, any disease process that affects the optic nerve can affect RNFL thickness measures on OCT. Furthermore, cellular supportive structures such as vasculature and glial components are also measured as part of the RNFL thickness, and the RNFL is not solely representative of neuronal tissue.<sup>[1]</sup>



**Figure 4:** Macular OCT shows ganglion cell complex atrophy (no color/green = within normal limits; yellow = outside the 95% normal limit; red = outside the 99% normal limit) in homonymous patterns corresponding to the bilateral homonymous visual field defects (correlated HVF are flipped upside-down and eyes reversed, underneath). Large arrows identify areas associated with the right homonymous superior quadrantanopia; small arrows show areas associated with the left homonymous superior paracentral scotomatous defects

Therefore, macular GCC analysis has been increasingly utilized for detecting retrograde trans-synaptic degeneration. To our knowledge, there are few reports of isolated macular changes in patients with confined post-geniculate lesions.<sup>[9-11]</sup> In a study examining 64 eyes of patients with homonymous hemianopia and post-geniculate lesions, 65% had topographic macular thinning corresponding to the visual field defect, and of those, 59% also had a reduced peripapillary RNFL.<sup>[18]</sup> Interestingly, 25% of patients with these macular changes had a normal RNFL, and 9% of the eyes had only RNFL thinning.<sup>[18]</sup> The authors concluded that the combination of macular GCC and RNFL thinning was most sensitive in detecting retrograde trans-synaptic degeneration, but patients with normal or borderline peripapillary RNFL could still demonstrate GCC thinning. Post-geniculate lesions exhibited macular thinning on OCT approximately 5 months after the lesion, as opposed to as early as 1 month in pre-geniculate lesions involving the optic tract and chiasm.<sup>[18]</sup> Our patient, who presented with isolated macular changes at 3 years following post-geniculate strokes, supports the postulate that peripapillary RNFL

OCT measurements alone are less useful at detecting retrograde trans-synaptic degeneration.

More accurate characterizations of the ophthalmic findings following brain insults are important for multiple reasons. There is growing interest in the role of OCT in prognosticating visual field recovery following stroke. A comparative study between patients with posterior strokes with and without retinal changes may be of value in understanding the significant differences in long-term visual outcomes. In addition, detecting these changes can be beneficial in diagnosing visual field defects in patients who are unable to participate or tolerate functional visual field testing.<sup>[4]</sup> Finally, OCT is a powerful tool that may help establish the acuteness of lesions incidentally found on imaging by providing an estimation of insult timing based on the degree of degeneration seen in the retina. While the specific kinetics of degeneration have been reported with variances, there is evidently a period of normalcy prior to degeneration, and perhaps additional research will elucidate this curve. This may ultimately be beneficial in determining the strategy and timing of rehabilitative interventions for these patients.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his de-identified images and other clinical information to be used for teaching and research purposes. The patient understands that his name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

This work is supported in part by NIH/NEI core grant P30-EY06360.

### Conflicts of interest

BSC is the recipient of the VJ Chapman Research Fellowship awarded by the New Zealand Neurological Foundation. VB and NJN are consultants for GenSight Biologics. NJN is a consultant for Santhera Pharmaceuticals and Stealth BioTherapeutics. The remaining authors declare no relevant conflicts of interest.

## References

1. Kardon RH. Role of the macular optical coherence tomography

scan in neuro-ophthalmology. *J Neuroophthalmol* 2011;31:353-61.

2. Goldby F. A note on transneuronal atrophy in the human lateral geniculate body. *J Neurol Neurosurg Psychiatry* 1957;20:202-7.

3. Miller NR, Newman SA. Transsynaptic degeneration. *Arch Ophthalmol* 1981;99:1654.

4. Dinkin M. Trans-synaptic Retrograde Degeneration in the Human Visual System: Slow, Silent, and Real. *Curr Neurol Neurosci Rep* 2017;17:16.

5. Jindahra P, Petrie A, Plant GT. Retrograde trans-synaptic retinal ganglion cell loss identified by optical coherence tomography. *Brain* 2009;132:628-34.

6. Jindahra P, Petrie A, Plant GT. The time course of retrograde trans-synaptic degeneration following occipital lobe damage in humans. *Brain* 2012;135:534-41.

7. Park HY, Park YG, Cho AH, Park CK. Transneuronal retrograde degeneration of the retinal ganglion cells in patients with cerebral infarction. *Ophthalmology* 2013;120:1292-9.

8. Goto K, Miki A, Yamashita T, Araki S, Takizawa G, Nakagawa M, *et al*. Sectoral analysis of the retinal nerve fiber layer thinning and its association with visual field loss in homonymous hemianopia caused by post-geniculate lesions using spectral-domain optical coherence tomography. *Graefes Arch Clin Exp Ophthalmol* 2016;254:745-56.

9. Yamashita T, Miki A, Iguchi Y, Kimura K, Maeda F, Kiryu J. Reduced retinal ganglion cell complex thickness in patients with posterior cerebral artery infarction detected using spectral-domain optical coherence tomography. *Jpn J Ophthalmol* 2012;56:502-10.

10. Mitchell JR, Oliveira C, Tsiouris AJ, Dinkin MJ. Corresponding ganglion cell atrophy in patients with postgeniculate homonymous visual field loss. *J Neuroophthalmol* 2015;35:353-9.

11. Hokazono K, Ribeiro Monteiro ML. Homonymous quadrantic macular ganglion cell complex loss as a sign of trans-synaptic degeneration from occipital lobe lesion. *Am J Ophthalmol Case Rep* 2019;13:76-9.

12. Johns P. Cellular mechanisms of neurological disease. In: Johns P, editor. *Clinical Neuroscience*. Ch. 8. London, England: Churchill Livingstone; 2014. p. 91-103.

13. Wang JT, Medress ZA, Barres BA. Axon degeneration: Molecular mechanisms of a self-destruction pathway. *J Cell Biol* 2012;196:7-18.

14. Vanburen JM. Trans-synaptic retrograde degeneration in the visual system of primates. *J Neurol Neurosurg Psychiatry* 1963;26:402-9.

15. Hoyt WF, Rios-Montenegro EN, Behrens MM, Eckelhoff RJ. Homonymous hemioptic hypoplasia. Fundoscopic features in standard and red-free illumination in three patients with congenital hemiplegia. *Br J Ophthalmol* 1972;56:537-45.

16. Beatty RM, Sadun AA, Smith L, Vonsattel JP, Richardson EP Jr., Direct demonstration of transsynaptic degeneration in the human visual system: A comparison of retrograde and anterograde changes. *J Neurol Neurosurg Psychiatry* 1982;45:143-6.

17. Porrello G, Falsini B. Retinal ganglion cell dysfunction in humans following post-geniculate lesions: Specific spatio-temporal losses revealed by pattern ERG. *Vision Res* 1999;39:1739-45.

18. Mühlemann F, Grabe H, Fok A, Wagner F, Brügger D, Sheldon CA, *et al*. Homonymous hemiatrophy of ganglion cell layer from retrochiasmatal lesions in the visual pathway. *Neurology* 2020;94:e323-9.