Acta Ophthalmologica

Acta Ophthalmologica 2018

Preferential atrophy of the central retinal ganglion cells in homonymous hemianopia due to acquired retrogeniculate lesions demonstrated using swept-source optical coherence tomography

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doi: 10.1111/aos.13644

Editor,

Optical coherence tomography (OCT) studies of acquired occipital lobe lesions in humans have demonstrated corresponding inner retinal thinning with the use of time-domain OCT (TD-OCT) (Jindahra et al. 2009), and later, with the use of spectral domain OCT (SD-OCT) (Yamashita et al. 2012). In the present study, we analysed the whole macular area in eyes with homonymous hemianopia by high-penetration swept-source OCT (SS-OCT; DRI OCT-1 Atlantis, Topcon, Tokyo, Japan) and produced maps of the three macular inner retinal layer thicknesses (μm): (i) the macular retinal nerve fibre layer (mRNFL), (ii) the ganglion cell layer and inner plexiform layer (GCL + IPL) and (iii) the ganglion cell complex (GCC; mRNFL + GCL + IPL) thicknesses. The software program calculates the average retinal thickness of the mRNFL, GCL + IPL, GCC and the total for each 2 × 1.5 mm grid square of the 12 × 9 mm scan area. The macular retinal thickness parameters (centred on the macula) were divided vertically into the hemianopic and unaffected sides, and the averaged data between the two eyes were used for further quantitative analyses.

We examined 19 patients [male, $n = 9$; female, $n = 10$; age, 38–78 years (mean 60.5 years)] with unilateral retrogeniculate lesions and 56 age-matched normal control subjects [male, $n = 30$; female, $n = 26$; age, 20–82 years (mean, 56.2 years)]. The time between the SS-OCT measurement and the onset of brain lesions ranged from 1 month to 8.0 years (mean, 3.2 years). The age, sex and refraction values of the patients and the normal control subjects did not differ to a statistically significant extent ($p = 0.3834$, 0.7913 and 0.8657, respectively; age and refraction: unpaired Mann–Whitney *U*-test; sex: chi-squared test). In the eyes with homonymous hemianopia, each of these thicknesses of the hemianopic side was significantly thinner in comparison to normal eyes (Table 1). The macular inner retinal thicknesses on the hemianopic side of the central 2 × 3 mm area were significantly thinner than those in the unaffected sides (Table 1). A regression analysis revealed a negative linear relationship (linear regression, $R^2 = 0.605$, $p = 0.001$) between the time after stroke and the GCL + IPL thickness on the hemianopic side of the central 2 × 3 mm area. The GCL + IPL and GCC thicknesses of the wide angle 6 × 9 mm area on the hemianopic side of the patients with stroke were significantly thinner than those in normal subjects and those on the unaffected side (Table 1). The area under the receiver operating characteristic curve (AUC) values of the central 2 × 3 mm area GCL + IPL and the GCC thickness for discriminating between the brain lesion group and the normal control group were significantly greater than those in the wide angle 6 × 9 mm area (Table 2).

Our results using SS-OCT confirmed the observations of the previous studies using TD-OCT and SD-OCT, in that the inner retina showed statistically significant thinning corresponding to the affected visual hemifields in patients with acquired retrogeniculate damage. In addition, an area analysis revealed that the thinning predominantly occurred in the most central retina, close to the fovea. The latter finding is

Table 1. The macular thickness parameters in patients with homonymous hemianopia and normal controls, as measured by swept-source optical coherence tomography (SS-OCT) instruments (μm, Mean ± SD).

	2 × 3 mm area			6 × 9 mm area			2 × 3 mm area		6 × 9 mm area	
	Hemianopic side of hemianopes	Unaffected side of hemianopes	Normal controls	Hemianopic side of hemianopes	Unaffected side of hemianopes	Normal controls	p value[a]	p value[b]	p value[a]	p value[b]
mRNFL	24.3 ± 6.2	25.8 ± 4.2	28.5 ± 5.3	41.8 ± 9.4	42.2 ± 9.6	48.6 ± 33.3	0.0313	0.0018	0.2954	0.0042
GCL + IPL	63.7 ± 9.5	73.1 ± 7.9	82.8 ± 5.6	43.6 ± 2.7	45.0 ± 3.0	49.2 ± 15.6	0.0002	0.0001	0.0010	0.0001
GCC	86.9 ± 13.7	99.0 ± 11.4	111.4 ± 8.4	85.3 ± 10.0	87.1 ± 11.0	97.8 ± 32.3	0.0002	0.0001	0.0141	0.0001
Total	265.5 ± 13.7	273.2 ± 12.2	293.0 ± 14.6	222.9 ± 9.7	226.2 ± 14.6	240.5 ± 41.4	0.0010	0.0001	0.0872	0.0001

GCC = ganglion cell complex, GCL = ganglion cell layer, IPL = inner plexiform layer, mRNFL = macular retinal nerve fibre layer.
[a] Comparison of the macular thickness parameters of the hemianopic side and the unaffected side (Wilcoxon signed-ranks test).
[b] Comparison of the macular thickness parameters of the hemianopic side in patients with homonymous hemianopia and normal eyes (Mann–Whitney U-test).

Table 2. The area under the receiver operating characteristic curve (AUC) analysis using the SS-OCT-based measurement of the macular thickness on the hemianopic side in patients with homonymous hemianopia.

	AUC (standard error)		
	2 × 3 mm area	6 × 9 mm area	p value[a]
mRNFL	0.734 (0.082)	0.720 (0.073)	0.8407
GCL + IPL	0.981 (0.013)	0.912 (0.034)	0.0132
GCC	0.982 (0.012)	0.876 (0.049)	0.0242
Total	0.945 (0.024)	0.902 (0.046)	0.2818

GCC = ganglion cell complex, GCL = ganglion cell layer, IPL = inner plexiform layer, mRNFL = macular retinal nerve fibre layer.
[a] Comparison of the macular thickness on the hemianopic side in the 2 × 3 mm and 6 × 9 mm areas.

consistent with the results of experimental studies in primates, in which the selective loss of small ganglion cells projecting to the parvocellular layers of the lateral geniculate nucleus was observed after occipital lobe ablation (Weller et al. 1979; Cowey et al. 1989; Weller & Kaas 1989; Johnson & Cowey 2000). The similarity between animal experiments and human studies suggests that the retinal thinning of the OCT is—at least in part—due to trans-synaptic retrograde degeneration.

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A new mutation in enhanced S-cone syndrome

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doi: 10.1111/aos.13205

Editor,

The enhanced S-cone syndrome (ESCS) is an autosomal-recessive retinal degeneration associated with *NR2E3* mutation, which depresses the rod system, L-cone and M-cone and induces night blindness, an abnormal electroretinogram, cystoid maculopathy and degenerative changes of the vascular arcades (Marmor et al. 1990; Audo et al. 2008; Kanda & Swaroop 2009).

We report about a 9-year-old boy in regular general health who presented due to a visual decrease at lower ambient lights for 1 year. Ophthalmologic investigations were performed, and for genetic analysis, 167 genes responsible for different forms of retinal diseases were subsequently screened. The coding regions and flanking intronic regions were enriched using Agilent in-solution technology and sequenced using the Illumina HiSeq2500 system. Data analysis was focused first on previously described or pathogenic variants according to American College of Medical Genetics and Genomics (ACMG) guidelines (Richards et al. 2015) and extended to unknown variants in genes containing one variant of the first class.

The patients' medical examination, including laboratory testing of angiotensin converting enzyme (ACE), antinuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), rheumatoid factor (RF), protein immunoelectrophoresis, human leukocyte antigen B27 (HLA-27), cytomegalovirus (CMV), human immunodeficiency virus (HIV), toxoplasma gondii, epstein-barr-virus (EBV), brucella, borellia burgdorferi, treponema pallidum, candida, toxocara canis, tuberculosis and bartonella henselae, and immunoglobulin M (IgM) for herpes simplex virus (HSV) und varicella zoster virus (VZV) were regular, but positive as regards immunoglobulin G (IgG) of HSV and VZV. Best corrected visual acuity (BCVA) was 0.5 in both eyes, and anterior chambers were morphologically regular, respectively. Vitreous cells were absent. Nummular drusen-like spots were visible along the perimacular vascular arcades and also detectable with autofluorenscence photography (Fig. 1A; Spectralis OCT, Heidelberg Engineering, Germany). Fluorescein angiography revealed no leakages while macular spectral domain tomography (Spectralis OCT) bilaterally showed a cystoid macular oedema (Fig. 1B). Full-field electroretinography presented with reduced a- and b-wave amplitudes in scotopic conditions (Fig. 1D). As orally administered methylprednisolone, or acetazolamide, did not influence retinal morphology or BCVA remarkably, genetic