Patterns of Neurodegeneration in Macula Differs in Multiple Sclerosis Subtypes: a Voxel-Based Morphometry Study with Optical Coherence Tomography

Su-Chun Huang, Simone Guerrieri, Marco Pisa, Gloria Dalla Costa, Federica Esposito, Letizia Leocani

Department of Neurology and INSPE- Institute of Experimental Neurology, Scientific Institute and University Hospital San Raffaele, Milan, Italy

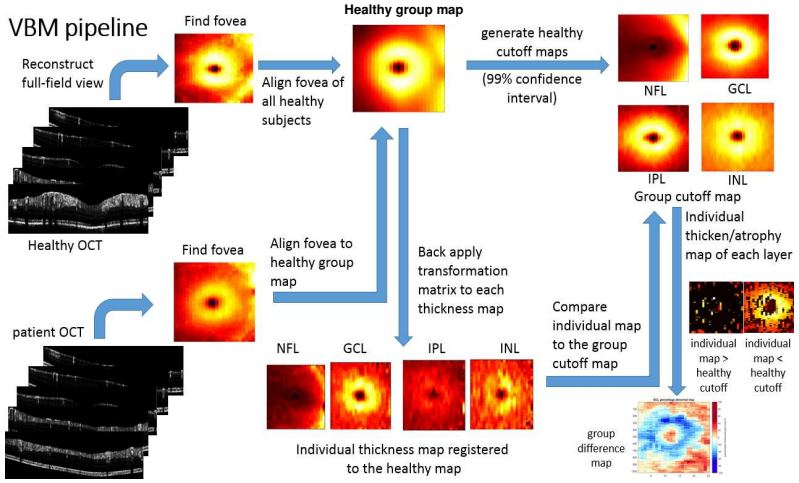
Introduction

Neurodegeneration of multiple sclerosis (MS) can be measured with optic coherence tomography (OCT), as thinning of peripapillary retinal nerve fiber layer (pRNFL), or as reduced total macula volume (TMV) [1]. The macula scan can be further segmented into ganglion cell layer (GCL), inner plexiform layer (IPL), and inner nuclear layer (INL), which are plausible markers for neuronal loss, dendritic loss, or ongoing inflammation [2]. Unlike traditional method yields only several averaged values of the whole image, voxel-based morphometry (VBM) can visualize and compare the whole macula map, therefore can be more sensitive in detecting focal lesions [3]. Here we applied VBM to macula OCT in different types of MS in early stage of the disease and compare the results with traditional pRNFL analysis.

Methods

Three groups of patients with CIS, RRMS, PPMS and fifteen healthy subjects were enrolled. Peripapillary (for pRNFL) and Macula volume scans were performed and segmented with Heidelberg Spectralis OCT. The segmented thickness maps of macula RNFL, GCL, IPL, and INL were registered to generate group maps with VBM and 99 percent confidence interval was calculated as the cutoff. Eyes with optic neuritis (ON) were excluded. Individual maps were compared with the group maps and voxels with thickness above/under the cutoff were considered as thicken/atrophy. Ultimately, the difference maps of the patient groups were generated, the value in each voxel represents how many percentage of patients showed thicken/atrophy at the certain location.

	CIS (N = 10 pt)	RRMS (N = 10)	PPMS (N = 10)	Healthy (N = 15)
Gender	1M / 9F	7M / 3F	8M / 2F	3M / 12F
Age (y)	32,1 ± 8,22	34,7 ± 8,99	47,0 ± 7,55	28,4 ± 3,88
Disease Duration (y)	1,13± 1,15	2,1 ± 1,31	2,7 ± 1,34	N/A
pRNFL (µm)	92,9 ± 5,51	94,8 ± 8,31	94,5 ± 10,38	100,2 ± 9,51



Results

Among the 30 patients (50 non ON eyes), 1 eyes showed borderline atrophy and 2 eyes showed borderline swelling in pRNFL analysis. No group difference was found. However, all the patients showed focal RNFL atrophy of macula compared with the healthy (figure 1). Further, macula GCL, IPL atrophy and INL thickening were found in all three patient groups (figure 2), which the lesion area increased from CIS to RRMS to PPMS. The atrophy of GCL in RRMS located mainly at nasal-inferior macula, while in PPMS was at temporal-superior. Further, thickening of INL in a specific area (located at nasal macula) was found in only 40% CIS group but 100% RRMS and PPMS.

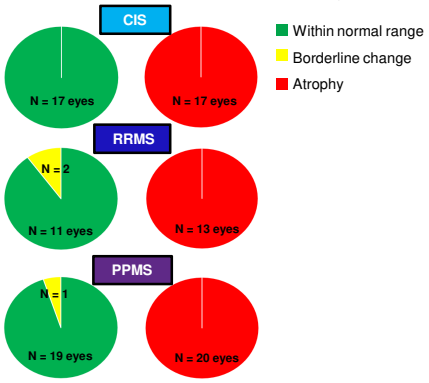


Figure 1. Abnormal Rate Detected with pRNFL and Macula RNFL (non ON eyes). In patients groups, most the pRNFL thickness were still within normal range, only 3 eyes showed borderline change, while focal atrophy of macula RNFL was detected among all the patients with macula VBM.

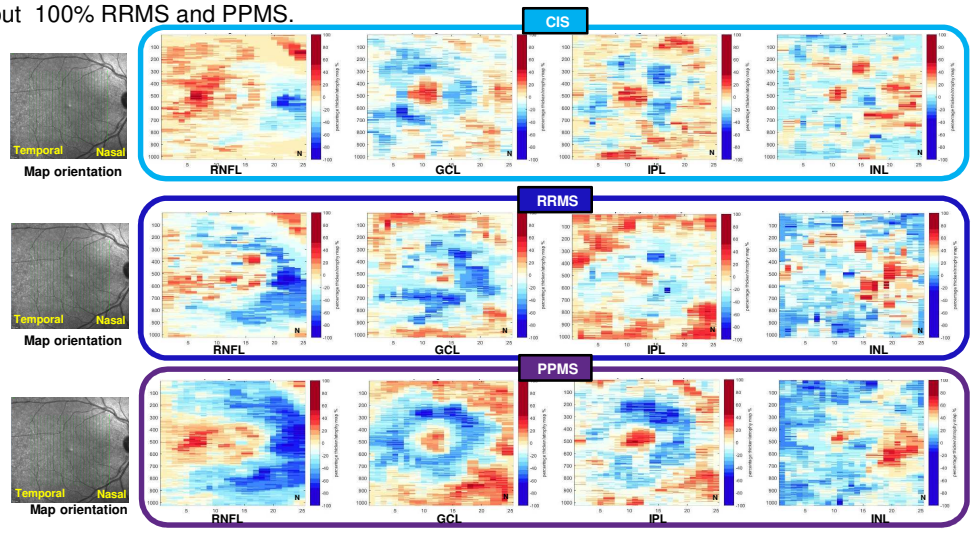


Figure 2. Group Difference Maps of Macula VBM. *The group difference maps compared with the healthy cutoff of RNFL, GCL, IPL, and INL were generated of the three patient group respectively. Red: Voxels which are thicken compare to healthy cutoff. Blue: voxels which are atrophy compare to healthy cutoff. Color bar: percentage eyes showed thickening/atrophy. N: nasal.*

Discussions and Conclusions

Our results suggest that macula OCT is more sensitive in detecting neurodegeneration in MS patients than peripapillary RNFL scans. Also, RRMS and PPMS patients showed different patterns of neurodegeneration within macula GCL, which could be a marker for early diagnosis of progressive patients. Long-term follow-up is needed to examine if the nasal INL thickening of macula can be a marker to predict the converter from CIS to MS.

References

[1] Petzold A, de Boer JF, Schippling S, Vermersch P, Kardon R, Green A, Calabresi PA, Polman C. Lancet Neurol 2010(9): 921-32. [2] Petzold A, Balcer LJ, Calabresi PA, Costello F, Frohman TC, Frohman EM, Martinez-Lapiscina EH, Green AJ, Kardon R, Outteryck O, Paul F, Schippling S, Vermersch P, Villoslada P, Balk LJ, IMSVISUAL E-E. *Lancet Neurol* (2017)16: 797-812. [3] Antony BJ, Chen M, Carass A, Jedynak BM, Al-Louzi O, Solomon SD, Saidha S, Calabresi PA, Prince JL. *Proc SPIE Int Soc Opt Eng (2016)*:9788.

Conflict of Interests

No conflict interest to be declared for any of the authors.

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