The analysis of optic pathway does not disclose correlations between white matter damage and neurodegeneration in very early multiple sclerosis

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Introduction. The optic pathway was suggested to be a prototype system to investigate trans-synaptic degeneration in multiple sclerosis (MS).

Objective. To investigate possible relationships between white matter (WM), cortical and retinal damage in a very early phase of MS

Materials an Methods.

Study population: 43 patients with clinically isolated syndrome or very early relapsing remitting MS (CIS/eRRMS; mean disease duration 3.4±3.0 mths) and 31 matched HC were studied. Patients were divided into optic neuritis positive (ON+, n.10) or ON- (n.33) on the base of clinical presentation (Table 1). MRI protocol: MRI examination included 3D-T1 and 3D-FLAIR) sequences. Global cortical thickness (gCTh), pericalcarin CTh (V1-CTh) and white matter volume (WMV) were analysed by means of Freesurfer on 3D-T1 scans. Optic radiation morphology (OR) and volume (ORV) were reconstructed on the base of the Jülich's Atlas (Figure 1). White matter lesion volume (WMLV), OR-WMLV and percent WM damage (WMLV/WMV=WMLV% and OR-WMLV/ORV=ORWMLV%) were obtained by 3D-FLAIR image segmentation. OCT protocol: optic coherence tomography (OCT) included the analysis of macular volume (MV), global peripapillary retinal nerve fiber layer (g-RNFL) and the 6 *fundus oculi*'s sectors (temporal, T-RNFL; temporal superior, TS-RNFL; nasal superior, NS-RNFL; nasal, N-RNFL; nasal inferior, NI-RNFL, temporal inferior, TI-RNFL). The retina of both eyes was analyzed. The eyes of ON+ were further divided into affected (aON+) or not (naON+).

	Patients				Controls	
	Overall	**ON+**	**p**	**ON-**	**hC-OCT**	**hC-MRI**
number	**43**	**10**	**-**	**33**	**31**	**28**
age (years) mean ± dev.st (range)	35.0 ± 10.3 (18-59)	34,3 ± 10,7 (22-56)	0.8	35.2 ± 10.4 (18-59)	35.4 ± 9.1 (25-59)	36.1 ± 14.1 (66-14)
female/male ratio	1.65	1.67	1.0	1.65	1,4	3,7
disease duration (months) mean ± dev.st (range)	3.4 ± 3.0 (0-10)	4.5 ± 4.1 (0-10)	0.2	3.1 ± 2.6 (0-9)	n.a.	n.a.
EDSS median (range)	2.0 (1.0 ± 4.0)	2.0 (1.0 ± 4.0)	0.5	2.0 (1.0 ± 3,5)	n.a.	n.a.
delay onset-MRI (months) mean ± dev.st (range)	3.4 ± 3.0 (0-10)	4.5 ± 4.1 (0-10)	0.2	3.1 ± 2.6 (0-9)	n.a.	n.a.
delay OCT-MRI (months) mean ± dev.st (range)	1.1 ± 1.7 (0-8)	1.6 ± 1.2 (0-3)	0.3	1,0 ± 1,8 (0-8)	n.a.	n.a.

Table 1. *Demographic and clinical features of the patients included in the study.*

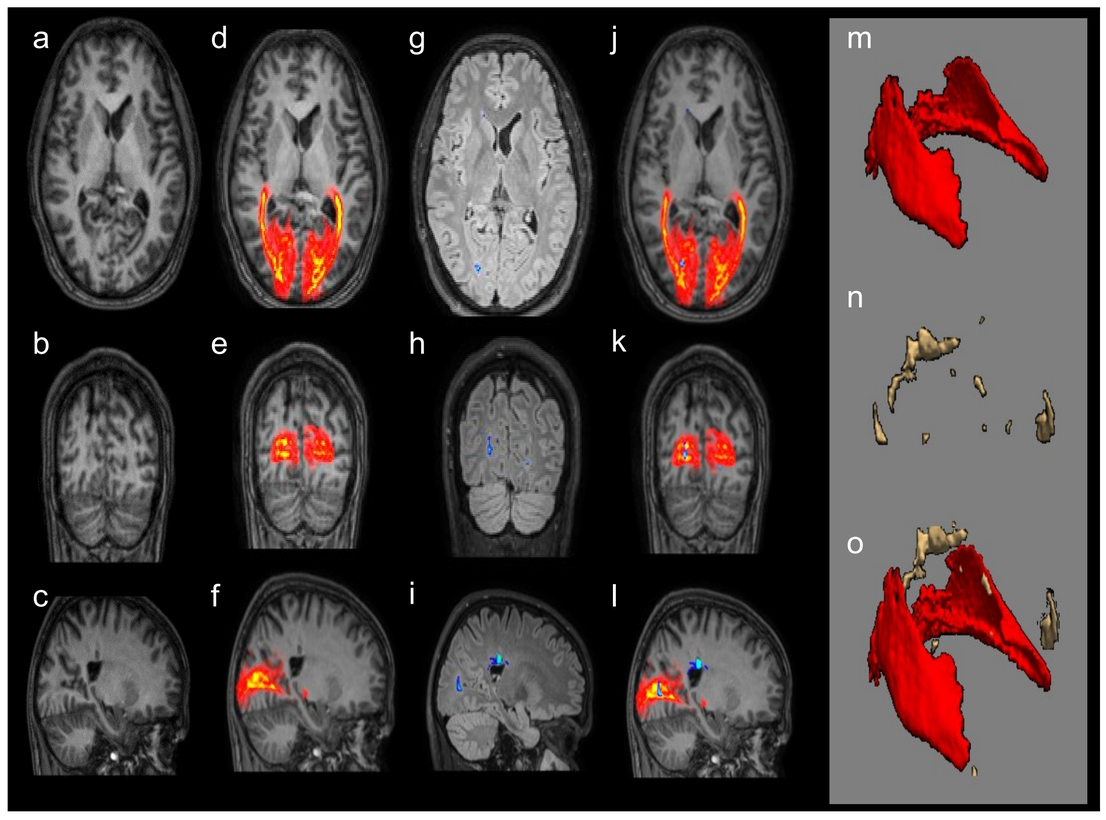

Figure 1. T1-3D (Figure a, b, c) images were recorded by the software fsl within the space NMI in order to reconstruct three-dimensionally the optical radiation applying the Jülich probabilistic atlas (threshold: 0.20, Figure d, e, f). The volume of interest (VOI) corresponding to the areas of white matter demyelination were selected through the program mricron by a team of neurologists using MRI 3D-FLAIR sequences (Figure g, h, i). These volumes were calculated by counting the voxels in each VOI and have been converted to mm³, defining the total WMLV. Finally, ORWMLV (Figure j, k, l, o) was calculated by the software by merging the 3D reconstruction of optical radiation (Figure m) with the VOI (Figure n).

Results.

MRI data. ON+ had an higher WMLV, OR-WMLV, WMLV% and OR-WMLV% than ON- (Figure 2), while gCTh, pericalcarin CTh and the ratio between WMLV% and ORWMLV% did not differ between the two groups.

No correlation between gCTh or pericalcarin CTh and OR-WMLV or OR-WML% was observed in both groups.

OCT data. Compared to HC and ON- eyes, aON+ presented a significant thinning of T-RNFL (p<0.0001) and TI-RNFL (p<0.0001) (Figure 3). The multivariate analysis failed to disclose any correlation between OCT data and MRI WM and cortex parameters.

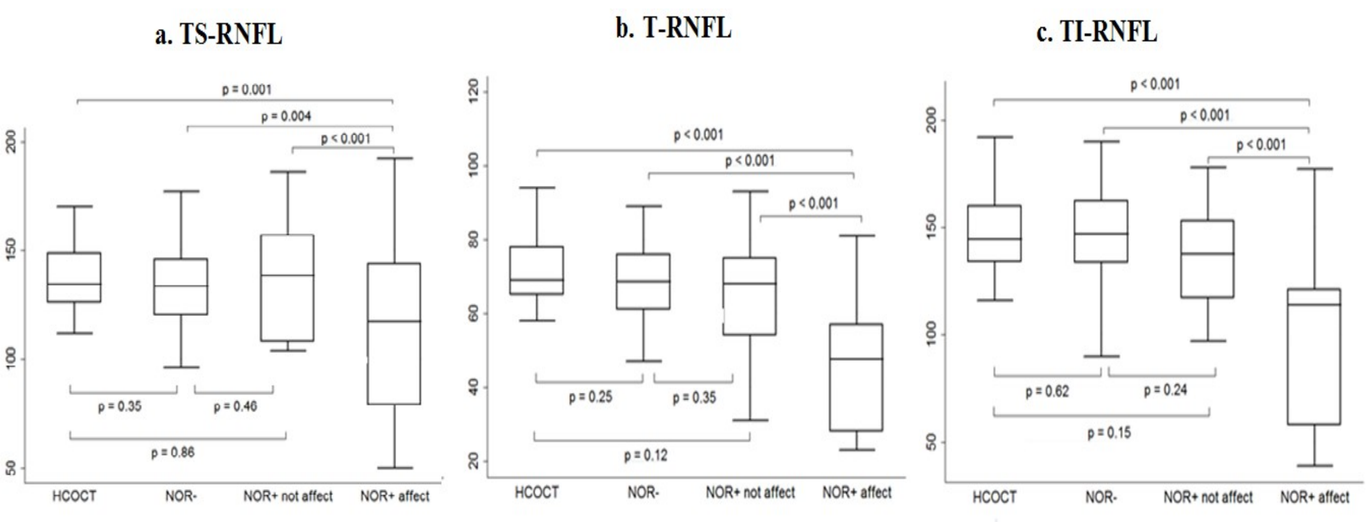

Figure 3. Temporal field RNFLs.

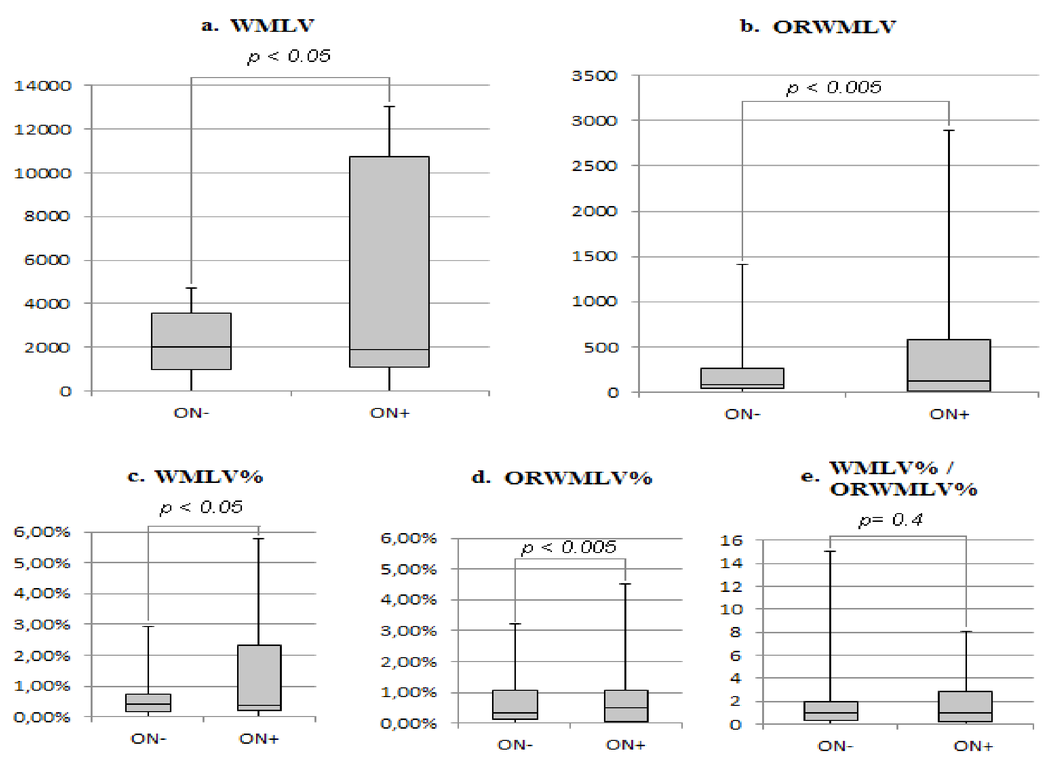

Figure 2. White Matter MRI parameters in ON+ and ON-. ON+ presented significantly higher ORWMLV and ORWMLV% and an increased WMLV and WMLV% compared to ON-. The ratio did not differ between the two groups.

Conclusions. No relationship between WM, cortical and retinal damage in both ON+ and ON- CIS/eRRMS patients could be demonstrated. In CIS/eRRMS ON+ patients lesions in both optic nerve and WMOR were not associated to a reduction of pericalcarin Th, a finding that do not support the presence of a significant trans-synaptic degeneration in early disease phases.