Neurodegeneration in Multiple Sclerosis: comparison between clinical, neuropsychological, MRI and Optical Coherence Tomography parameters

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BACKGROUND AND OBJECTIVE

Optical Coherence Tomography (OCT) enables rapid, non-invasive in vivo measurement of retinal nerve fiber layer (RNFL) thickness, reflecting axonal density within the optic nerve. There is still lack of concordance about the use of OCT in clinical routine as a surrogate measure of brain atrophy.

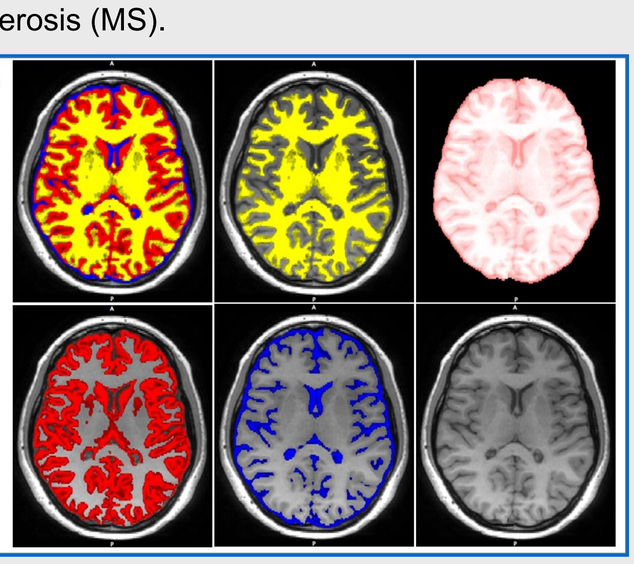
Objective: To investigate the role of OCT as possible predictor of disability, cognitive impairment and neurodegeneration in Multiple Sclerosis (MS).

MATERIAL AND METHODS

- We recruited patients affected by MS according to validated criteria at the Neurological Department of the University of Palermo.
- Patients performed Stratus OCT- 3 Zeiss to assess RNFL and GCS measurements.
- Nearly 18 months later, the same patients were re-evaluated. Clinical and cognitive status was assessed also using an extensive neuropsychological battery exploring attention, executive functions and working memory, verbal and visuo-spatial memory, visuospatial functions and language and BICAMS (Brief International Cognitive Assessment for Multiple Sclerosis). Patients performed all subtests of the Italian standardized version.
- Subjects underwent a single-time-point brain scan using a 1.5T MRI unit; an isotropic 3D-FSPGR T1w sequence was used for brain tissue volume estimation (normalized for subject head size) with tissue-type segmentation by the use of FSL's package SIENAX.
- We collected information about disease status, EDSS, relapse rate and current and former therapies.

Figure 1 Axial Multi-Planar Reconstructions (MPRs) from the sagittal 3D Fast Spoiled GRadient echo (FSPGR) T1-wheighted sequence used for the voxel-based analysis (sequence specifications: spatial resolution 1.1x1.1x0.6mm; acquisition matrix 256x256; TR 12.368ms; ET 5.088ms; IT 450ms; FA 90; ETL 1; NEX 1).

a) Normalized raw data;
b) Extracted brain volume from normalized raw data in pink;
c) Cerebral Spinal Fluid (CSF) volume in blue;
d) Grey matter (GM) in red;
e) White Matter (WM) in yellow;
f) All the extracted brain tissues superimposed to the normalized raw data.



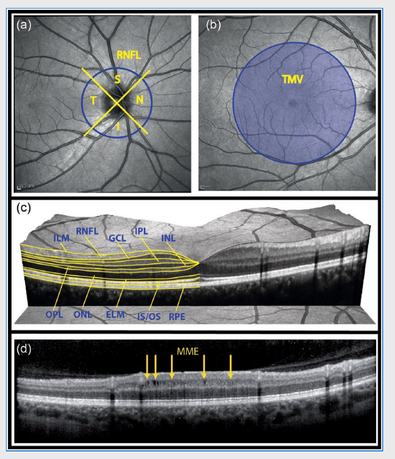


Figure 2. Optical Coherence Tomography (OCT)

RESULTS

- Thirty patients (20 women; 27 RR, 2 SP) were recruited for the study.
- Patients were divided into two groups considering if they were affected by a previous optic neuritis (ON yes) or not (ON no).
- Ten patients performed the MRI scan
- Twenty-two patients were on therapy (5 Interferon beta 1 a, 8 Natalizumab, 8 Fingolimod and 1 azathioprine) and 8 patients don't take any specific therapy

Table 1. Clinical, demographic and OCT characteristic in SM with previous optic neuritis or not

Variables	ON (yes) n=17 Mean±DS o (%)	ON (no) n=13 Mean±DS o (%)	p
Men/woman	5/12	5/8	0,6
Age at onset	25,8±7,2	35,9±8,4	0,001
Age at interwiev	40,5±9,2	43,9±9,2	0,4
Disease duration	14,9±9	8,0±6,1	0,02
Number of relapese/5 years	3,2±2,3	2,1±1,2	0,2
EDSS	5,1±2,1	3,0±2,2	0,006
Mean RNFL OD	85,0±17	102,8±8,4	0,001
Mean RNFL OS	80,0±19,6	101,9±9	0,0009
GCL Total	57,6±7,3	64,8±5	0,1

Table 2. Neuropsychological profile in SM with previous optic neuritis or not

Variables	ON (yes) n=17 Mean±DS o (%)	ON (no) n=13 Mean±DS o (%)	p
Education (years)	12±3	13±5,02	0,5
Mini Mental State Examination	27,5±3,9	29,3±1,2	0,1
Digit span	5,1±1,2	5±1	0,8
Rey Auditory Verbal Learnig Task Immediate recall	32,5±11,9	33,7±8,9	0,8
Rey Auditory Verbal Learnig Task Delayed recall	5,7±3,2	6±2,9	0,8
Letter Fluency	27,2±10,3	26,5±7,6	0,8
Catecorig Fluency	29,7±8,7	35,1±6,5	0,1
Rey's Complex Figure copy	27,5±9,3	32,4±5,1	0,1
Rey's Complex Figure recall	8,7±4,5	12,1±7,5	0,2
Raven's color progressive matrices	26,03±4,2	27,5±4,8	0,4
Visual Search	40,7±16,7	51,9±6,4	0,03
BICAMS Symbol Digit Modalities Test	30,5±7,3	35,2±9,3	0,1
California verbal learning Test	37,8±10,4	38,9±16,9	0,8
Brief visuospatial Memory Test-revised	40,7±10,7	39,7±7,8	0,8

Table 3. MRI results

Variables	ON (yes) *Mean±DS*	ON (no) *Mean±DS*	p
GMA (norm.)	652942,0±81847,1	778254,1±98837,2	0,07
WMA (norm.)	767521,2±20035,7	778611,7±24660,5	0,5
GPBF Sienax tot (norm.)	420463,2±98797,9	556865,7±104109,2	1,0
GMA (unnorm.)	455849,1±57986	544476,2±80698,2	0,1
WMA (unnorm.)	537206,1±49449,6	545838,5±56095,8	0,8
GPBF (unnorm.)	993055,2±96404,8	10903134,7±118587	0,8

GPBF: global parenchimal brain fraction; **GMA**: gray matter atrophy; **WMA**: white matter atrophy.

Variables	OR	95% CI	p
Executive Functions	1,009	0,95-1,07	0,26
Attention	0,98	0,93-1,04	0,47
Memory	1,14	0,99-1,30	0,07
Language	1,04	0,96-1,13	0,31
Visuo-spatial functions	1,04	0,98-1,1	0,25

Table 4. Model of *logistic regression including each variable and considering the presence or not of a previous ON.*

- **We observed also a significant correlation between previous ON and grey matter atrophy (B 2.45, DS B 0.99, p 0.04) independent by cognitive performances.**

DISCUSSION AND CONCLUSION

- .The present study confirms previous data indicating an association between a previous optic neuritis and RFNL thickening.
- We didn't observe a significant association with cognitive performances.
- We observed a significant association also between RFNL thickness and grey matter atrophy independent by neuropsychological performances
- .There is a need to increase the sample of the study and for longitudinal studies to further clarify the role of OCT as a surrogate marker of degeneration.

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