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MAGNETIC RESONANCE

Optic radiation damage in multiple sclerosis is associated with visual dysfunction and retinal thinning – an ultrahigh-field MR pilot study

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Abstract
Objective To investigate posterior visual pathway damage in multiple sclerosis using ultrahigh-field magnetic resonance imaging (MRI) at 7 Tesla (7 T), and to determine its correlation with visual disability and retinal fibre layer (RNFL) damage detectable by optic coherence tomography (OCT).
Methods We studied 7 T MRI, OCT, functional acuity contrast testing (FACT), and visually evoked potentials (VEP, n= 16) in 30 patients (including 26 relapsing-remitting MS and four clinically isolated syndrome patients) and 12 healthy controls to quantify RNFL thickness, optic radiation lesion volume, and optic radiation thickness.
Results Optic radiation lesion volume was associated with thinning of the optic radiation ($p<0.001$), delayed VEP ($p=0.031$), and visual disability indicated by FACT ($p=0.020$). Furthermore, we observed an inverse correlation between optic radiation lesion volume and RNFL thickness ($p<0.001$), including patients without previous optic neuritis ($p<0.001$).
Conclusions Anterior visual pathway damage, but also (subclinical) optic radiation integrity loss detectable by 7 T MRI are common findings in MS that are mutually affected. Given the association between optic radiation damage, visual impairment, and increased VEP latency in this exploratory study of a limited sample size, clinicians should be aware of

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acute lesions within the optic radiation in patients with (bilateral) visual disturbances.

Key Points

- *Focal destruction of the optic radiation is detectable by 7 T MRI.*
- *Focal optic radiation damage is common in MS.*
- *Optic radiation damage is associated with RNFL thinning, detectable by OCT.*
- *Optic radiation damage is associated with delayed VEP and visual dysfunction.*
- *RNFL thickness in non-optic neuritis eyes correlates with optic radiation demyelination.*

Keywords Multiple sclerosis · Magnetic resonance imaging · Retinal nerve fibre layer · Optic radiation · Trans-synaptic degeneration

Introduction

Multiple sclerosis (MS) is considered an inflammatory demyelinating and neurodegenerative central nervous system disorder. The underlying pathophysiology of axonal loss [1–3], however, has remained unclear, impeding the development of neuroprotective drugs.

The visual system is highly susceptible to MS related damage. Visual disturbances are frequent and cause serious disability, but imaging of the visual pathway posterior to the optic chiasm – comprising the optic radiation (OR) – has remained challenging due to technical limitations. The OR as part of the posterior visual pathway transmits information from the ipsilateral temporal and contralateral nasal hemiretinae, projecting from interneurons of the lateral geniculate nucleus (LGN) to the striate cortex. The LGN, in turn, directly receives axons from retinal ganglion cells. These large and highly myelinated axons pass through the periventricular white matter [4, 5], being susceptible to focal inflammatory damage in MS.

Diffusion tensor imaging (DTI) recently enabled the examination of OR integrity loss, but could not visualise focal demyelination. Today, owing to increased susceptibility effects and a very high signal-to-noise ratio, high resolution magnetic resonance imaging (MRI) at 7 Tesla (7 T) [6, 7] picks up alterations of MS brain parenchyma with great anatomical details, and hence facilitates the distinction between MS and non-MS lesions, e.g. of vascular origin [8–10], lesions in patients with Susac syndrome [11, 12], or neuromyelitis optica [13]. Moreover, 7 T MRI delineates the OR against surrounding white matter with great distinction. The anatomical details revealed by T2* weighted (T2*w) fast low angle shot (FLASH) provides an opportunity not only to visualise, but also to quantify focal damage causing OR integrity loss.

In addition, retinal nerve fibre layer (RNFL) thinning detectable by optical coherence tomography (OCT) [14–16], delayed visually evoked potentials (VEP) [17], and visual dysfunction [16, 18] also in MS patients without a history of ON may indicate subclinical damage to the visual system.

Realising the excellent visibility of the OR in 7 T T2*w MRI, we aimed to quantify (subclinical) focal damage and atrophy of the optic radiation in MS. Furthermore, we investigated whether focal damage of the OR is related to delayed VEP, impaired visual function, OR thickness, and RNFL thinning in eyes with and without history of ON.

Materials and methods

Study participants

Patients with relapsing-remitting (RR) MS according to the 2010 panel criteria [1], or with clinically isolated syndrome (CIS) without history of ON were consecutively and prospectively enrolled between March 2010 and December 2012 at the Clinical and Experimental MS Research Center at the Charité-Universitaetsmedizin Berlin, Germany. Inclusion criteria were 1) RRMS disease course or patients with CIS who were aged 18 to 80 years and 2) informed written consent. Exclusion criteria were any contraindication for ultrahigh-field MRI at 7 T (e.g. pacemaker, claustrophobia or pregnancy). Patients underwent 7 T MRI at the Berlin Ultrahigh Field Facility (B.U.F.F.). In addition, OCT, functional acuity contrast testing (FACT), and VEP were performed during the routine workup at the NeuroCure Clinical Research Center (NCRC) by investigators that were not involved in MR imaging. VEP, OCT, and FACT investigators were not blinded with respect to clinical data. OCT and FACT were usually performed on the same day or within two days. Patients showing an interval between MRI and OCT measurements of more than 200 days were excluded after initial inclusion, and VEP measurements with an interval between MRI and VEP of more than 6 months were not further analysed. A flow chart is presented in Fig. 1. RRMS patients with time since first symptoms of up to 3 years were defined as “early MS”. Neurological disability was rated by the Expanded Disability Status Scale (EDSS) [19], and history of ON was determined clinically by patient history and medical records. Healthy controls comparable to our patient cohort with regard to sex and age served as controls to investigate potential age and sex effects, and underwent 7 T MRI, OCT, and FACT. The study was approved by the local ethics committee and was conducted in accordance to the Declaration of Helsinki in its currently applicable version. All participants gave informed written consent.

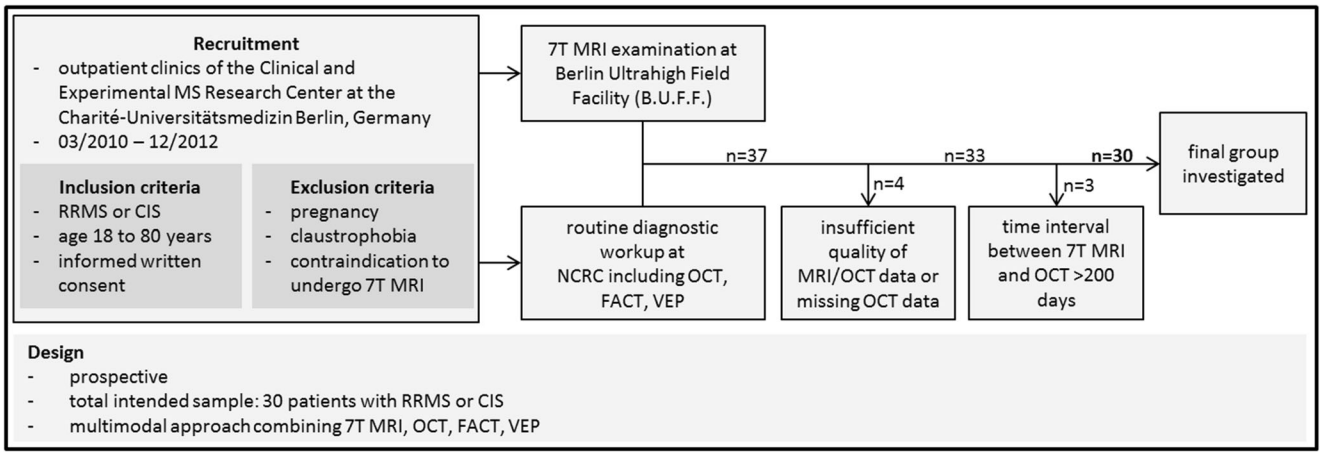

Fig. 1 Flow chart

MRI data acquisition

Ultrahigh-field MR images were acquired on a 7 T whole body MR system (Magnetom, Siemens, Erlangen, Germany), using a 24-channel RF coil equipped with one transmit channel (Nova Medical, Wilmington, MA, USA). The imaging protocol included axial T2*w FLASH (TE=25 ms, TR=1,820 ms, acquisition time 12:11 min, in plane spatial resolution=0.5×0.5 mm^2, slice thickness=2 mm), and fluid attenuated inversion recovery imaging (FLAIR; TE=90 ms, TR=16,000 ms, TI=2,925.5 ms, acquisition time=12:50 min, in plane spatial resolution=1.0×1.0 mm^2, slice thickness=3 mm).

Algorithms quantifying optic radiation damage

The lesion fraction affecting the OR on consecutively pseudonymised T2*w images was manually delineated by a trained observer unaware of paraclinical (VEP, OCT, FACT) data, and was confirmed by a clinical neuroradiologist with more than 10 years' experience in clinical and scientific MS imaging, who was not aware of paraclinical (VEP, OCT, FACT) and clinical data (disease duration, EDSS) (Fig. 2a–d). For obvious reasons, blinding the MRI reader to MS diagnosis was not possible. The optic radiation lesion volume was calculated using the OsiriX software package (OsiriX Foundation, Geneva, Switzerland, version 3.8.1). The T2*w optic radiation thickness of each hemisphere was quantified in separate analyses (Fig. 2e): for each subject, seven continuous axial slices characterised by a high inter-individual comparability were selected: (i) one slice tangential to the inferior splenium of the corpus callosum and superior of the vein of Galen, (ii) three slices in parallel inferior to the first slice, and (iii) three slices in parallel superior to the first slice. A straight line was plotted orthogonal to the interhemispheric fissure and in parallel to the posterior part of the splenium. This line was propagated to the inferior slices. The observer then measured the OR thickness twice in an anterior and posterior position (Fig. 2e). Finally, the mean OR thickness for each slice and hemisphere was calculated.

Image analyses

T2 lesion count was determined by counting all T2*w hyperintense brain lesions with a volume of at least three voxel at T2*w FLASH, showing a corresponding signal hyperintensity on FLAIR. Virchow-Robin spaces were excluded by their tubular appearance and FLAIR hypointensity. Lesions were masked manually using OsiriX integrated ROI functions. Third ventricle width and bicaudate ratio were assessed as described previously [20, 21], calculated as a mean value derived from three measurements. Two healthy controls were excluded for technical reasons (missing/modified MR sequence affecting measures of third ventricle width). Automated procedures for brain volume quantification, as routinely used in conventional field strengths, suffered mainly from the magnetic field heterogeneities and thus could not be reliably applied.

MR images of nine MS patients were analysed by a second blinded observer (CR) to estimate inter-rater reliability as a two-way mixed average measure intra-class correlation coefficient (ICC), using the consistency model. We achieved a high inter-rater reliability for OR thickness (ICC=0.972), OR volume (ICC=0.882), third ventricle width (ICC=0.976) and bicaudate ratio (ICC=0.938).

Optical coherence tomography

OCT was performed on non-dilated eyes using a spectral-domain (SD)-OCT device (Heidelberg Spectralis® SD-OCT, Heidelberg Engineering, Heidelberg, Germany). All participants were examined with the peripapillary ring scan, measuring the RNFL thickness encircling the optic nerve head in a diameter of approximately 3.4 mm, forming a composition of

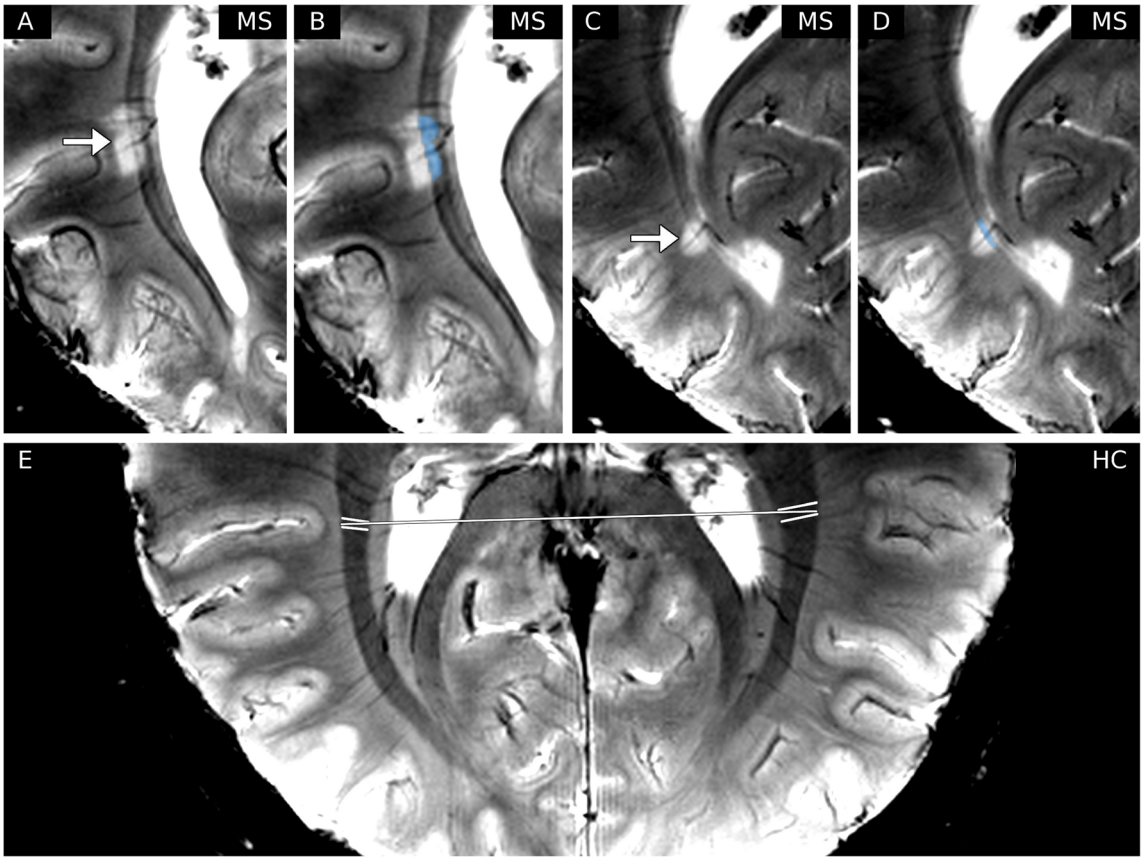

Fig. 2 Focal optic radiation damage. Lesions in MS patients (white arrow) commonly affected the optic radiation as shown here in two exemplary patients (**a**–**d**); healthy controls (**e**) did not present with any OR pathology. The quantified part of the white matter lesion covering the optic radiation was marked in blue for better visualisation (**b**, **d**). In addition, optic radiation thickness was measured in four positions in each of seven consecutive slices (**e**). *Sequence parameters*: 7 T T2*w FLASH, TE=25 ms, TR=1,820 ms, spatial resolution=(0.5×0.5) mm^2

1536 A-scans. All scans were reviewed for correct centring and image quality according to the OSCAR-IB guidelines without knowing 7 T MRI data [22].

Visual perception and VEP

FACT was acquired by trained investigators using the Optec 6500 P system (Stereo Optical, Chicago, IL, USA) with the best correction under photopic conditions ('daylight' with target luminance value of 85 cd/m^2) not knowing 7 T MRI data, as previously described [23]. VEP measures were recorded from the Oz electrode against a Cz reference electrode following standard checkerboard stimulation. Between 40 and 80 recordings were averaged twice and P100 peak latency was measured.

Statistical analyses

The nasal, superior-temporal and inferior-temporal RNFL-sectors reflect visual information from both hemi-retinae [24]. Therefore, we calculated mean values from both eyes and brain hemispheres.

Group differences were assessed using Mann-Whitney U test (MWU) for age, bicaudate ratio, third ventricle width, RNFL, OR thickness, and Pearson's Chi squared test (alpha=0.05) for gender. A potential gender-related effect on OR thickness was analysed using MWU. Associations between the variables examined were investigated using Spearman's correlation and ranked partial correlation.

All analyses were performed in SPSS (version 20, IBM, Somers, NY, USA). *P*-values <0.05 were considered significant. All tests should be understood as exploratory data analyses, as no previous power calculation and adjustments for multiple testing were made.

Results

We prospectively enrolled 30 patients and 12 healthy controls. The patient cohort included 26 RRMS patients, including nine patients with early MS and four patients with CIS. The demographic details are summarised in Table 1. FACT was analysed in 29 patients and 11 healthy controls (median time interval

Table 1 Cohort description

		Healthy controls	Patients	ON	nON
n		12	30	11	19
Sex	female [n]	6	12	4	8
	Chi^2		p=0.55	p=0.51	p=0.67
Age (years)	mean ± SD	34±11	35±8	38±6	34±9
	range	20-54	19-49	29-46	19-49
	MWU		p=0.54	p=0.29	p=0.86
Time since MS diagnosis (years)	mean ± SD	n/a	4.6±4.5	5.6±5.4	3.8±3.8
	range		0.2-14.7	0.2-14.7	0.2-11.3
Time since first symptoms (years)	mean ± SD	n/a	6.4±6.5	9.1±7.9	4.8±5.1
	range		0.1-27.7	0.2-27.7	0.1-14.1
EDSS	Median, range	n/a	1.5	1.5	1.5
			0-4.5	1-4.5	0-4.5

Key: ON, patients with a history of acute optic neuritis; nON, patients without any history of acute optic neuritis; EDSS, Expanded Disability Status Scale; MWU, Mann-Whitney U test; Chi2, Pearson's Chi squared test; n/a, not applicable; SD, standard deviation. *p*-values describe differences to healthy controls

between MRI and OCT/FACT 2.6 months, range 0 – 6.4). VEP was performed in 16 patients (median time interval between MRI and VEP 3.2 months, range 0 – 5.2). Group differences for patients/healthy controls as well as ON subgroups are presented in Table 2. In total, we detected 898 white matter lesions in patients with RRMS and CIS on T2*w FLASH images (mean ± SD 30±33, range 1 – 116). Sixteen white matter lesions visible in three healthy controls did not exhibit unusual characteristics. It is noteworthy that all analyses mentioned below should be understood as exploratory in nature.

Evaluation of the optic radiation

T2*w imaging at 7 T visualised the OR with great anatomical detail. Hence, all further analyses were made on 7 T T2*w MR images: the mean OR thickness was 3.9 mm in healthy controls (Fig. 2e), and significantly lower in patients (2.9 mm, p<0.001). No gender differences in OR thickness were observed in healthy controls (p=0.49) or patients (p=0.82), nor did OR thickness decrease with age in healthy controls (p=0.27) or patients (p=0.22). Likewise, no association between RNFL and OR thickness was found in healthy controls.

Evaluation of optic radiation damage in MS

We found 120 OR lesions (mean OR lesion volume ± SD 142 ±201, range 0 – 632 mm^3) in 24/30 patients that were often characterised by a central vein considered typical of MS (Fig. 2a–d) [7, 13, 25]. Involvement of the OR was already detectable in 10 of 13 CIS and early MS patients (mean OR lesion volume ± SD 106±184, range 0 – 531 mm^3).

Quantification of T2*w OR lesion volumes (Table 2) confirmed an inverse association between OR lesion volume and thickness (supplemental Fig. 1; Spearman's-Rho -0.614, p<0.001). This correlation between OR atrophy and OR lesion volumes remained significant after correcting for i) brain atrophy reflected by two methods, bicaudate ratio (p=0.001) and third ventricle width (p=0.001), and ii) for global T2w lesion count (p=0.013).

Association between optic radiation damage, OCT, and VEP in MS

We observed an inverse relationship between OR lesion volume and RNFL thickness (Spearman's-Rho -0.640, p<0.001, Figs. 3, 4a). Decreased RNFL thickness was also associated with increased bicaudate ratio as measure of brain atrophy (p=0.045), and higher T2 lesion count (p=0.017). The observed association of RNFL thickness reduction with increasing OR lesion volume remained significant after correcting for brain atrophy determined by both third ventricle width (p<0.001) or bicaudate ratio (p<0.001), and T2 lesion count (p=0.002). Likewise, we observed a significant correlation between OR thickness reduction and RNFL thinning (Spearman's-Rho 0.499, p=0.005, adjusted for bicaudate ratio p=0.018, adjusted for third ventricle width p=0.013, Fig. 4b). Furthermore, VEP latency was prolonged with increasing OR lesion volumes (Spearman's-Rho 0.606, p=0.013).

Optic radiation damage is associated with visual dysfunction in MS

When further exploring visual dysfunction in MS patients by automated testing of high and low contrast acuity (Table 2), we observed an association of high OR lesion volume with poor low contrast sensitivity under photopic conditions (Spearman's-Rho -0.429, p=0.020). However, the relationship between FACT and OR lesion volume is not necessarily an independent phenomenon. It might well be explained by RNFL thinning, that was also associated with poor low contrast sensitivity (p=0.004). Consequently, statistical analysis

Table 2 Group differences

		Healthy controls	All patients	ON	nON
n		12	30	11	19
T2 lesion count	mean ± SD	1±4	30±33	42±37	23±28
	range [n]	0-13	1-116 ***p*<0.001**	6-116 ***p*<0.001**	1-96 ***p*<0.001**
Bicaudate ratio	mean ± SD	10.8±1.7	8.6±1.9	8.1±2.1	8.8±1.7
	range [mm]	8.6-14.3	5.5-14.5	5.5-11.2	7.0-14.5
	MWU		***p*=0.001**	***p*=0.016**	***p*=0.002**
Third ventricle width	mean ± SD	2.3±1.1	3.7±1.4	4.4±1.6	3.3±1.2
	range [mm]	0.8-4.8	1.8-7.8	2.6-7.8	1.8-5.6
	MWU		***p*=0.001**	***p*=0.001**	***p*=0.012**
RNFL	mean ± SD	98±9	87±15	84±19	89±13
	range [um]	83-119	59-116	59-116	60-109
	MWU		***p*=0.022**	*p*=0.059	***p*=0.039**
VA	mean ± SD	1.3±0.3	1.1±0.3	1.1±0.2	1.1±0.3
	range	0.8-1.6	0.4-1.6	0.8-1.6	0.4-1.6
			p=0.052	*p*=0.104	*p*=0.087
FACT 85 cd/m^2	mean ± SD	2.0±0.1	1.8±0.3	1.8±0.2	1.9±0.3
	range	1.8-2.2	1.0-2.3 ***p*=0.041**	1.5-2.3 ***p*=0.005**	1.0-2.3
					p=0.256
VEP latency	n	n.d.	16	4	12
	mean ± SD		108±9	114±7	106±9
	range [ms]		93-123	107-122	93-123
OR lesion volume	mean ± SD	0	142±201	226±241	93±161
	range [mm^3]		0-632	0-632	0-490
OR thickness	mean ± SD	3.9±0.6	2.9±1.0	2.7±1.2	3.0±0.8
	range [mm]	3.0-4.9	0.6-4.7	0.6-4.3	1.4-4.7
	MWU		*p*<0.001	*p*=0.011	*p*=0.001

Key: ON, patients with a history of optic neuritis; nON, patients without any history of acute optic neuritis; RNFL, retinal nerve fibre layer; MWU, Mann-Whitney U test to assess differences between patient subgroups and healthy controls; VA, visual acuity; FACT, functional acuity contrast testing; VEP, visual evoked potentials; OR, optic radiation; SD, standard deviation. Because of technical limitations, we excluded unilateral visual acuity in one patient and unilateral FACT in one control. N.d., not determined. *P*-values describe differences to healthy controls. *P* values <0.05 are considered significant and thus shown in bold

revealed no significant association between OR lesion volume and FACT when factoring RNFL thickness in the statistical model (p=0.407).

Optic radiation and retinal damage in patients without history of optic neuritis

OR damage was detectable in 14 of 19 patients without previous history of ON (nON, Table 2). Surprisingly, those patients also showed pronounced OR thinning (mean OR thickness 3.0 mm) in comparison to healthy controls (mean OR thickness 3.9 mm, p=0.001, Table 2). Likewise, OR lesion volume in nON was correlated inversely with thinning of both, the RNFL (p<0.001) and the OR (p=0.035). This relationship was still significant when correcting for T2 lesion count (p<0.001), brain atrophy determined by bicaudate ratio (p=0.001), and third ventricle width (p=0.003). Accordingly, we observed a dependency between higher measures of OR lesion volume and impaired visual function (FACT p=0.009) as well as delayed VEP (p=0.024) in nON.

Optic radiation and retinal damage in patients with history of optic neuritis

History of simultaneous or sequential bilateral (n=7) and unilateral (n=4) ON was recorded in 11 MS patients. As expected, we did not observe any correlations between OR lesion volume and FACT, VEP, and RNFL measures in MS patients with a history of ON since ON itself may cause severe visual dysfunction and RNFL thinning.

Discussion

Ultrahigh-field MRI offers a distinct visualisation of the OR. Using dedicated morphological imaging of brain (7 T MRI) and retinae (OCT), as well as functional measures (FACT, VEP), we here investigated damage to the visual pathway in MS patients in comparison to healthy controls. We demonstrate that i) focal OR damage is present in earliest disease stages and in the majority of MS patients, and ii) the extent of

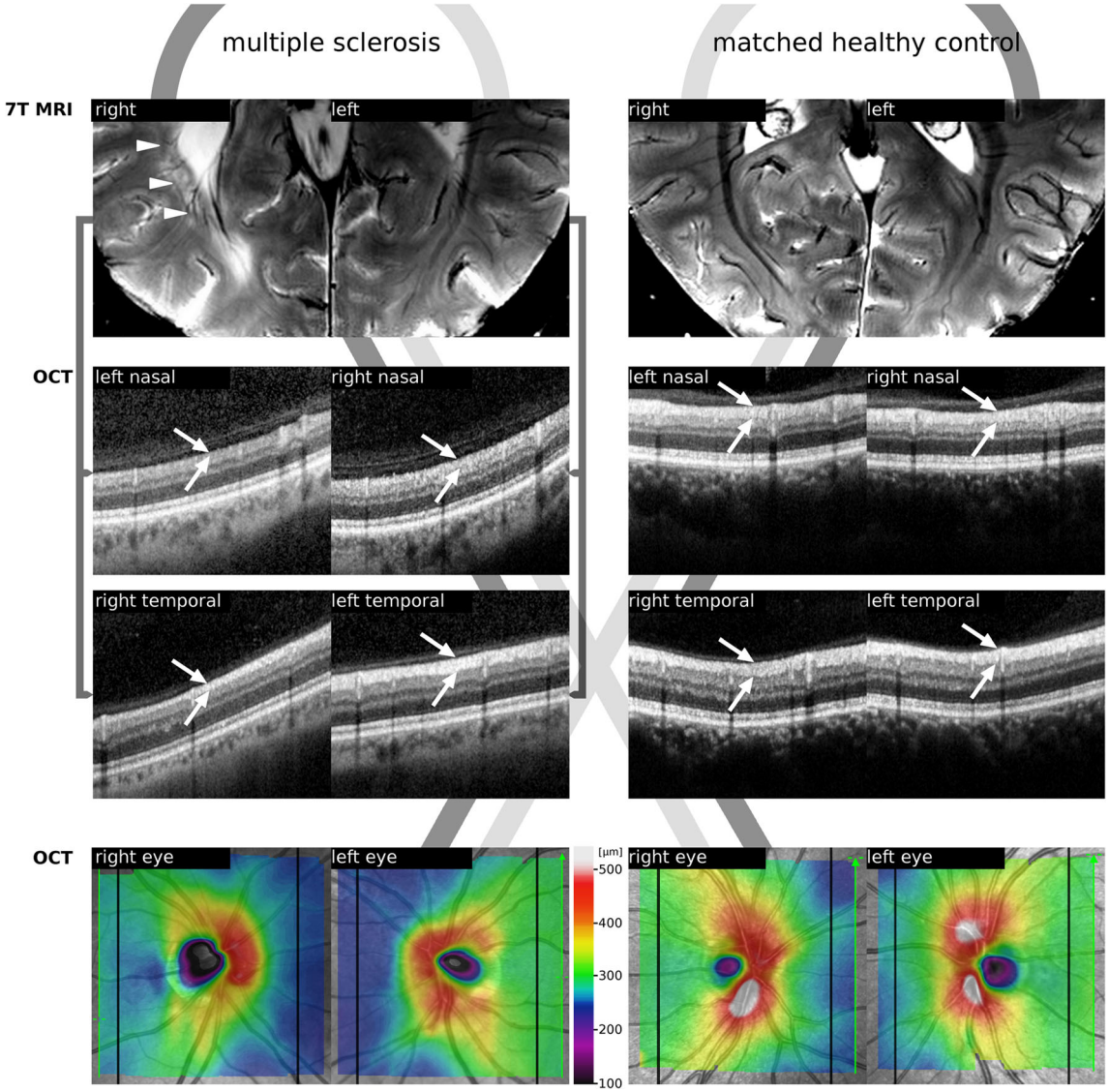

Fig. 3 Combined retinal and optic radiation damage in one exemplary MS patient. T2*w imaging visualises MS lesions of the atrophic right OR (*arrowheads*). The contralateral OR exhibits only minor abnormalities on 7 T T2*w images. OCT revealed corresponding RNFL thinning (*arrows*) of the ipsilateral temporal and contralateral nasal hemi-retinae. The nasal hemi-retina of the right eye and the temporal hemi-retina of the left eye present RNFL-thinning to a much lesser extent. One more speculative explanation for corresponding RNFL thinning is trans-synaptic degeneration remote from the damaged right OR. Following this assumption, bilateral optic neuritis was presumably misdiagnosed in this patient with bilateral visual disturbances and bilateral increased VEP latencies. However, we cannot exclude the possibility of independent phenomena simultaneously affecting the anterior and posterior visual pathway. *Sequence parameters*: 7 T T2*w FLASH, TE=25 ms, TR=1,820 ms, spatial resolution=(0.5×0.5) mm^2

focal damage to the posterior visual pathway is associated with thinning of the OR and retinal axonal degeneration.

A histological analysis of a post mortem specimen confirmed that the identified T2*w-hypointense periventricular structures indeed reflect the OR; however, in alignment with other reports [4, 26], these were negative in Prussian blue staining for iron (data not presented), a more common cause of T2*w signal extinction. Thus, the signal extinction of the OR observed at 7 T T2*w sequences may rather reflect anisotropic phase phenomena [27] caused by tightly packed, highly aligned axons with compact myelin. This phase phenomenon caused by high anisotropy may induce signal loss on T2*w imaging. 7 T gains from substantially increased susceptibility effects in comparison to lower field strengths [4, 5]. Consequently, 7 T T2* offers the unique potential to reveal very small focal lesions affecting the OR in a high in-plane spatial resolution.

A plausible explanation for the observed relationship between region-specific atrophy of the OR and occurrence of lesions within the OR is focal axonal trans-section within MS plaques, as reported by MRI and histological studies to occur in both, active and chronic MS lesions [6, 28].

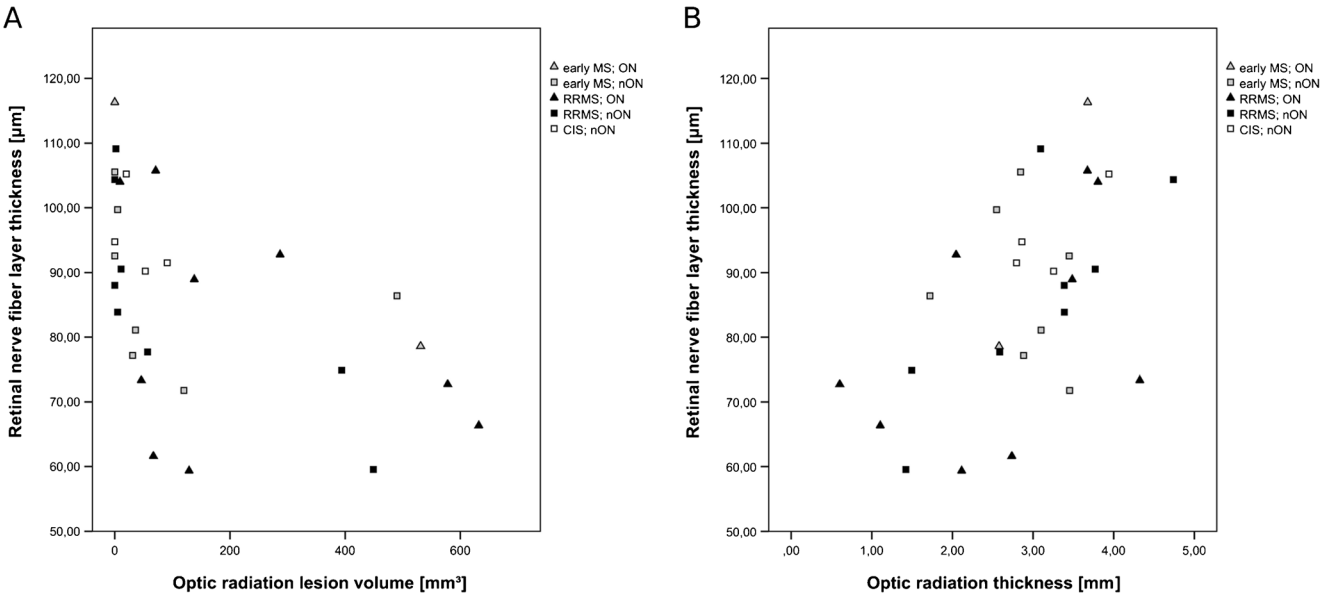

Fig. 4 Association of optic radiation damage with retinal nerve fibre layer thickness. Quantitative analysis revealed an association between the RNFL thickness and both, OR lesion volume (**a**), and OR thickness (**b**)

Although the cross-sectional design of this study may not answer questions about the causality, we hypothesise that our findings on retinal and OR degeneration result from subclinical and potentially independent damage of both, the anterior and the posterior visual pathway. In fact, primary retinal pathology in a small proportion of MS patients was recently discussed [29, 30]. Therefore, one could assume that the relationship between retinal and optic radiation damage results from a common underlying disease process causing axonal damage.

A more speculative explanation is trans-synaptic retrograde degeneration, a phenomenon controversially discussed for decades [31–40], induced by optic radiation damage causing retinal thinning detectable by OCT. In our study, the association between focal tissue destruction in the OR and thinning of the RNFL remained significant even when considering exclusively patients without a history of ON, indicating that retinal axonal degeneration in MS occurs partially independent of ON - a notion also supported by previous OCT studies [14–16, 41]. The fact that no association between OR damage and RNFL thinning was detectable in MS patients with ON supports this assumption as the latter itself may cause substantial RNFL destruction [42]. Furthermore, OR and retinal damage in our study kept their significant association when factoring global brain atrophy and total T2*w lesion load in the statistical models. Hence, clinical and subclinical damage to the anterior and posterior visual pathways appear linked to each other and contribute to the correlation between brain atrophy and retinal degeneration in MS [43, 44]. However, trans-synaptic degeneration in MS remains controversially discussed.

In addition, our data suggest that both retinal and OR damage can cause visual impairment which is in alignment with previous data demonstrating a correlation of T2*w lesion load [18] or DTI measures such as fractional anisotropy [45, 46] with visual dysfunction.

Future longitudinal studies are warranted to prove the causal relationship between OR damage and visual disability, since in our study the latter was statistically also explicable by RNFL thinning. Given the high number of OR lesions and the association between focal OR damage, visual disability, and delayed VEP in our study, it is nevertheless conceivable that an acute MS plaque within the OR affects visual function or VEP latency. Thus, a proven relationship between visual impairment and optic radiation integrity loss may directly impact clinical decisions.

Some limitations of our exploratory study of a limited sample size with multiple comparisons need to be addressed: Non-uniformities of the magnetic field at 7 T prevented us from performing automated computational white and grey matter volume measurements, nevertheless the reliability of the applied brain atrophy methodology was demonstrated before [20, 21]. We cannot exclude subclinical optic nerve damage, and the inferior part of the Meyer loop was not always visualised due to technical limitations. Furthermore, OR quantification may be influenced by MS lesions.

In summary, our study revealed a high prevalence of focal OR damage in MS from the earliest clinical stages correlating with visual dysfunction, VEP latency and retinal axonal damage. Hence, acute lesions affecting the optic radiation should be considered when diagnosing patients suffering from bilateral visual disturbances.

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Methodology: prospective cross sectional study performed at one institution.

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