ORIGINAL ARTICLE

Retinal Nerve Fibre Layer Thickness of Migraine Patients with or without White Matter Lesions

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ABSTRACT

The aim of this study was to determine whether retinal nerve fibre layer (RNFL) thickness is correlated with cerebral white matter lesions (WML) in migraine patients. Forty migraine and 40 healthy subjects were included in this study. The difference in RNFL thickness between the control and a migraine group with WML and a migraine group without WML were investigated using analysis of variance (ANOVA). A Tukey post hoc test was conducted to determine from which group the difference originated. Lower RNFL thicknesses were observed in the migraine patient group where WML was detected using magnetic resonance imaging (MRI), compared with the control group and with the migraine group with no WML. Statistically significant difference was found between the three groups in terms of RNFL thickness. Although there was a statistically significant difference between the control and the migraine group with WML detected with MRI, no statistically significant difference was found in terms of RNFL thickness between the control and the migraine group with no WML related to Tukey post hoc test. Moreover, there was a statistically significant difference between migraine patients with WML and patients without WML in terms of retinal nerve fibre layer thickness. The results indicate that reduction in RNFL detected via optical coherence tomography may be related to cerebral WML in migraine patients. Further studies by neurologists and ophthalmologists are necessary to determine the clinical relevance of the relation between RNFL and cerebral WML.

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Introduction

Migraine is a disabling neurological disorder, characterised by paroxysmal attacks of unilateral throbbing headache and neurological symptoms. Migraine affects up to 16% of the general population.^{1–3} There are several hypotheses about the pathogenesis of migraine: inherited alteration of brain excitability, intracranial arterial dilatation, recurrent activation and sensitisation of trigeminovascular pathway, and consequential structural and functional changes in genetically susceptible individuals.^{3–5}

As disturbances in the neurovascular system remain one of the mechanisms, the relationship between migraine and vascular events has been studied for many years.^{3,6} According to the literature, a high signal on T2-weighted magnetic resonance imaging (MRI) studies on migraine patients indicates an increase in subcortical white matter lesions (WML) due to chronic ischaemia.^{2,7–14} Also, there are studies supporting the ischaemic theory by focusing on the retinal nerve fibre layer

(RNFL) thickness detected by optical coherence tomography (OCT) on migraine patients and studies demonstrating that the retina and cerebral structure of migraine patients are affected.^{15–21}

In the present study, we used OCT to determine whether RNFL thickness is related to the presence of cerebral WML in migraine patients. Thus, we aimed to evaluate an anatomical relationship of RNFL thickness to MRI findings in migraine patients. With this study, migraine patients with WML detected in MR images in neurology clinics may be checked for possible thinning in RNFL.

Materials and methods

This is a prospective study; 40 patients with migraine with or without aura according to the criteria of the International Classification of Headache Disorders 3rd edition beta version and 40 age-matched healthy controls were chosen.¹ Patients with migraine and the control group were

recruited from the neurology clinic. MRI scans of all migraine patients were checked for WML, and OCT scans were conducted for RNFL thickness.

Institutional review board approval was obtained from the Bagcilar Research and Training Hospital, and the study was conducted in full accordance with all Declaration of Helsinki specifications. Informed consent was obtained from all patients.

Patients with diabetes mellitus, hypertension, cardiovascular and renal diseases, history of central nervous system disorders including brain tumors, infarction, encephalitis, epilepsy, Alzheimer's disease, head or eye trauma, and any type of headache except for migraine were eliminated from the study.

Control subjects were required to have had less than three headaches in the past year and never to have experienced a migraine attack. Patients with WML detected in MRI scans for other reasons were not included in this group.

All the participants underwent a complete ocular examination, including best-corrected visual acuity testing with Snellen charts, slit-lamp biomicroscopy, dilated fundus examination, pachymetry, and intraocular pressure (IOP) measurement using a Goldmann applanation tonometer. Following the clinical examination, patients with glaucomatous damage by increased intraocular pressure or by a secondary mechanism were excluded from the study. Eyes with retinal and optic disc pathology, high myopes (spherical equivalent less than or equal to -6.0 dioptres), glaucoma, dense cataract, or corneal opacity that made OCT imaging impossible and eyes previously subjected to intraocular surgery or ocular laser treatment were also excluded.

All patients who met the ophthalmological criteria were examined with a spectral-domain OCT

(Optos Spectral Domain OCT; UK). All scans were done using an internal fixation target in the OCT device. The fast RNFL scan protocol consisted of three consecutive 360° circular scans with a diameter of 3.4 mm centred on the optic disc. Mean RNFL thicknesses were examined in both eyes of migraine patients and the control group. Measurements from the right eye of migraine and control patients were included in the study.

Cranial MRI scans of the patients were obtained with 1.5-T system, FLAIR and T2 sequence, and the patients with WML were determined. In the study, white matter and basal ganglion lesions were classified according to the Age-Related White Matter Changes (ARWMC) scale. The ARWMC scale indicates the changes in the white matter related to age and also examines lesions observed in the basal ganglion. In this scale, WML and basal ganglion lesions of the patients are rated according to their sizes. For this purpose, hyperintense lesions are assessed during FLAIR and T2 sequences. The right and left hemispheres of the brain are divided and examined in five separate regions (Figure 1).²²

In this study, the participating groups are composed of the control group, the migraine patient group with WML, and the migraine patient group without WML. For statistical analyses, SPSS 17.0 for Windows package software (SPSS, Chicago, IL, USA) was used in this study. For all three groups, right eye RNFL average thickness was evaluated via OCT, and the differences between the groups were examined using analysis of variance (ANOVA). A Tukey post hoc test was carried out in order to determine from which group the differences originated.

Figure 1. This is a four-grade rating scale from MRI for punctate microvascular lesions in the white matter. Absence of lesions corresponds to grade 0; presence of non-confluent focal lesions corresponds to grade 1; presence of initially confluent lesions corresponds to grade 2; presence of diffuse confluent lesions corresponds to grade 3.

Table 1. Average retinal nerve fibre layer (RNFL) thickness and average data for all groups: migraine patients with white matter lesions (WML), migraine patients without WML, and control group.

Group	n	Mean RNFL thickness (micron)	SD	SE
Migraine—WML present	16	97.87	5.20	1.30
Migraine—WML absent	24	110.13	6.67	1.36
Control	40	107.69	8.07	1.27
Total	80	106.46	8.37	0.93

Results

Out of the 80 subjects selected for the study, 40 were migraineurs and 40 were controls, all meeting the inclusion criteria. Out of the 40 patients in the migraine group, 18 had migraine with aura and 22 had migraine without aura. There were no statistically significant differences between the migraineurs and the control subjects in sex and age ($p > 0.05$). The average age of the migraine patients was 35.7 ± 9.5 , and the average age of the control group was 40.9 ± 12.7 . WML was detected in 16 migraine patients, and basal ganglion lesions were not detected in any patient. Average data of all groups are presented in Table 1.

According to the performed statistical analyses, RNFL thicknesses were found to be smaller in the migraine patient group with WML detected in MRI scans compared with the control group and the migraine patient group without WML. ANOVA results indicate that there is a statistically significant difference between each of the three groups in terms of RNFL thickness ($p < 0.001$). According to the results obtained from the Tukey post hoc test, whereas there is a significant difference between the control group and the migraine patient group with WML detected in MRI scans ($p < 0.001$), there was no statistically significant difference found between the control group and the migraine patient group

without WML ($p = 0.391$). Additionally, a statistically significant difference in terms of RNFL thickness was found between migraine patients with WML and the migraine patient group with no WML ($p < 0.001$) (Table 2).

Discussion

The results of the present study demonstrate a relation between RNFL thinning and the cerebral WML in migraine patients. It has been detected statistically that the RNFL of migraine patients with WML is thinner compared with migraine patients with no WML and with the control group. In this study, we evaluated the relation between RNFL thickness and cerebral WML, using OCT and brain MRI.

Embryologically, the retina is an extension of the diencephalon, and both organs share a similar pattern of vascularisation during development.²³ There is a close anatomical correlation between both the macrovascular and the microvascular blood supply to the brain and the retina, and both vascular networks share similar vascular regulatory processes.^{23–27} There are studies about the microvascular changes in the retina reflecting strokes and vascular dementia.^{28,29}

There are also separate studies demonstrating that the retina and cerebral structure of migraine patients are affected. It has been shown that RNFL thinning occurs at different quadrants, and there are also studies regarding the relation between migraine and retrobulbar blood flow alterations.^{15–21}

According to Kara et al.,³⁰ the retrobulbar circulation and flow haemodynamics in the left vertebral artery may be altered in both headache and headache-free periods in migraineurs without aura. Glenn et al.³¹ reported a case of complicated migraine due to bilateral retinal infarction. Beversdof et al.³² reported recurrent branch retinal infarcts in association with migraine.

Table 2. Tukey post hoc test results.

Group A	Group B	Mean difference (A – B)	SE	p value
Migraine—WML present	Migraine—WML absent*	–12.26*	2.31	<0.001
	Control*	–9.81*	2.12	<0.001
Migraine—WML absent	Migraine—WML present*	12.26*	2.31	<0.001
	Control	2.44	1.85	0.391
Control	Migraine—WML present*	9.81*	2.12	0.000
	Migraine—WML absent	–2.44	1.85	0.39

Note. Results from multiple comparisons between migraine patients with white matter lesions (WML), migraine patients with no WML, and control group for right eye average retinal nerve fibre layer (RNFL) thickness detected by optical coherence tomography.

*Mean difference is significant at the 0.05 level.

On the other hand, the reported prevalence of cerebral WML in migraineurs ranges from 4% to 59% in selected studies. The pathological findings of these lesions have been attributed to microvascular damage.² In our study, WML was detected in 40% of the patients; the RNFL thicknesses of these patients were compared with those of migraine patients without WML and the control group. These results imply that cerebral WML may be related to the reduction in RNFL thickness in migraine patients.

WML are not specific to migraine, as previous studies indicate that WML are a result of chronic ischaemic damage, hypertension, advanced age, and other systemic diseases where subjects are more at risk for WML. Patients with systemic diseases were left out of this study for this reason. We also did not include patients who used medications causing vasoconstriction, such as triptans and compounds containing ergotamine. These medications can increase the risk of ischaemic vascular events in treated migraine patients.³³

In conclusion, reduction in RNFL detected via OCT was related to cerebral WML in migraine patients for this small group of patients. Larger series with follow-up periods would be better than cross-sectional studies. To the best of our knowledge, this study is the first in which MRI and OCT were used to evaluate the relation between RNFL thickness and WML. Further studies by neurologists and ophthalmologists are necessary to determine the clinical relevance of the relation between RNFL and cerebral WML. Migraine patients with WML detected in MR images in neurology clinics may need to be directed to ophthalmologists to check for possible thinning in RNFL.

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Declaration of interest

The author reports no conflicts of interest. The author alone is responsible for the content and writing of the article.

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