Retinal & choroidal alterations in migraine patients compared to normal healthy controls

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Research Article

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Abstract

Purpose: Migraine is an incapacitating neurovascular disorder which primarily affects the working age population. Researchers have postulated that the transient vascular alterations during each migraine attack, leads to ischemic damage in the eye which can be measured via optical coherence tomography (OCT).

Methods: We recruited 29 volunteers: 13 migraineurs (mean age 28±8.8 years; 12 female and 1 male) and 16 age-matched controls (mean age 26.6±6.9; 9 female and 7 male). All individuals underwent a detailed ophthalmic examination by a qualified optometrist and a Migraine Disability Assessment (MIDAS test). The investigators were blind to the migraine diagnosis. Retinal Nerve Fibre Layer (RNFL) thickness, Retinal Thickness (RT), Ganglion Cell Complex (GCL), ranging from the inner-limiting membrane to the inner plexiform layer, and Choroidal Thickness (CT) were measured using the *3D OCT-1Maestro*, Topcon, a Spectral Domain OCT (SD-OCT) device.

Results: In the migraine population average RNFL was lower for several parameters however, results did not reach statistical significance. A significant decrease in the right eye inferior parafoveal ganglion cell layer in the migraine group of patients (mean = 25.15, SD = 4.08) compared to normal healthy controls (mean = 28.81, SD = 4.85; t = (27) = 2.17, p = 0.039) was documented. No other ganglion cell layer or choroidal thickness reached significance. No significant relationship between ocular thickness parameters and either MIDAS score, migraine duration or aura diagnosis was found.

Conclusion: A significant decrease in the right inferior parafoveal ganglion cell layer for migraine patients was reported. All other parameters did not reach significance. This area of research would benefit from a systematic review and meta-analysis which includes the RNFL, GCL and choroidal thickness and examines the impact of migraine type and MIDAS score/grade is needed

Introduction

Migraine is the second leading cause of worldwide disability in the under fifties [1]. Eleven percent of the general population have frequent attacks [2] which are known to last anywhere between a few hours and several days. Women are three times more likely to be diagnosed with the condition [3], with some researches suggesting that it might be related to the normal hormonal variation over a woman's life time [4]. In the UK, migraine is estimated to result in a loss of approximately 25 million days from work or school [5] at an estimated conservative cost of £3.42 billion per year (headache disorders-not respected, not resourced). The exact aetiology behind migraine is not understood however, most clinicians consider it to be a neurovascular disorder involving the trigeminal-vascular pathway with associated autonomic nervous system dysfunction [6]. Researchers have postulated that stimulation of the sensory neurones originating in the trigeminal ganglion, innervates blood vessels from the meninges and cerebral arteries via the release of vasoactive neuropeptides [7]. The transient vasodilation of these structures activates the mechanical and chemical stimulation of the adjacent nociceptors, triggering migraine pain. The

perception of pain however, is known to vary significantly between individuals [8]. Treatments such as triptans are used to treat migraine through the vasoconstriction of meningeal vessels, decreased neurogenic inflammation, and reduced central nociception [9]. Researchers have documented an increased association between vascular disease and migraineurs [10–13]. Additionally, there is some suggestion that migraine is linked to endothelial dysfunction which is required to regulate vasomotor tone [14].

Because the retina is an embryological extension of the brain, it is likely that repetitive episodes of cerebral vascular fluctuations have ocular implications which can be measured in the optic nerve, retina and choroid. In normal tension glaucoma (NTG), the vascular theory suggests that is the haemodynamic alterations and not an increase intra ocular pressure, that lead to glaucomatous progression [15,16]. In migraineurs there are also reports of retinal ischemia, secondary to retinal artery occlusions [17–20]. An important area of research is therefore to investigate any potential relationship between recurrent migraine attacks and structural changes in the eye linked to transient episodes of ischemia. A meta-analysis has already analysed the retinal nerve fibre layer (RNFL) thickness in migraine patients compared to normal healthy controls [21]. The study included 1530 migraine patients and 1105 healthy controls and documented thinner RNFL in the migraine population, when measurements were taken during their interictal (between headaches) period via Optical Coherence Tomography (OCT). The impact of severity or duration of migraine on the RNFL was not assessed due to a limited sample size, and the authors concluded that more studies were needed to assess the value of OCT measurement in migraine patients. Elsewhere, there is some suggestion that choroidal thickness and ganglion cell layer is thinner in a proportion of migraineurs. [22–27]. Findings however, are inconsistent [28–30]. The aim of the present study was therefore to determine if either RNFL, ganglion cell layer or choroidal thickness varies in migraine patients compared to normal healthy controls and to examine if there is any relationship between severity and or duration of migraine.

Materials And Methods

Participants aged between 18 and 45 years old, were recruited at City, University of London between 2018 & 2019. The study received ethical approval by City, University of London's Optometry Proportionate Review Committee. Volunteers diagnosed with any ocular disease, amblyopia, previous eye surgery, neurological disorders, systematic diseases (such as diabetes, hypertension or heart disease), pregnancy or anti-epileptics treatments were excluded from the study.

Prior to enrolment in the study written informed consent was obtained for all volunteers, following the tenets of the Declaration of Helsinki. An anonymous questionnaire was completed by all volunteers. The questionnaire was developed according to the Headache International Society (HIS) criteria [31] and included a Migraine Disability Assessment Score (MIDAS). Volunteers were assigned to the control group if they reported less than 3 headaches in the past year and they had never experienced a migraine. In accordance with the (ICHD-3rd) [32] patients diagnosed with migraine were classified into those with and without aura. All volunteers were asked not to intake alcohol or caffeine 24 hours before their data

collection visit. Migraineurs were additionally asked to confirm that they had not experienced a migraine attack in the last 24 hours to ensure that they were examined during the interictal period. All data was collected at City, University of London. Patients from both groups were randomly assigned to either the morning or afternoon sessions to minimise the effect of choroidal thickness variation due to diurnal rhythm [33].

The following test were carried out monocularly by all patients. Best-corrected visual acuity was recorded using a LogMAR chart (Thomson Software Solutions). Ocular axial length was recorded using the Topcon Aladdin Optical Biometer and Corneal Topographer HW 3.0, visual fields were examined using the Humphrey Field Analyzer (HFA-3). Objective refraction was carried out and intraocular pressure (IOP) measurements were taken via the Topcon Auto Kerato-Refracto Tonometer (TRK-2P). Fundus photograph, peripapillary Retinal Nerve Fibre Layer (RNFL) thickness, Retinal Thickness (RT), Ganglion Cell Complex (GCL), ranging from the inner-limiting membrane to the inner plexiform layer, and Choroidal Thickness (CT) were measured using the *3D OCT-1Maestro*, Topcon, a Spectral Domain OCT (SD-OCT) device. The OCT measurements were performed following the protocol described by [34]. For each eye, the radial scan and 3D Disc analysis functionalities within the *3D OCT-1Maestro* software were used. Only scans with a signal of strength at least 5 or above were included in the analysis. The OCT 3D Disc analysis automatically calculated the foveal retinal thickness, the average RNFL thickness and the foveal ganglion cell complex. Choroidal thickness was determined using the software's *Caliper* function, which allows to take linear measurements on the image. The thickness was measured perpendicular from the outer edge of the hyperreflective RPE to the inner sclera. Measurements were taken at the central fovea and at approximately 750μm temporal and nasal to the fovea.

Results

Out of the 31 volunteers aged between 18 to 45 years old that were identified, 29 met the inclusion criteria. The population therefore consisted of 13 migraine-suffering volunteers (mean age 28 ± 8.79, 12 female and 1 male) and 16 normal healthy controls (mean age 26.6 ± 6.89, 9 female and 7 male). Among the 13 participants suffering from migraine: 61.5% (8/13) had migraine with aura; 38.5% (5/13) had migraine with no aura.

A Kolmogorov Smirnoff test was initially carried out to determine which data sets were normally distributed. Based on these results, either an independent T test or a Mann Whitney U was then used to determine any significant differences between the normal healthy controls and the migraine group during their interictal period. Analysis revealed that neither age, gender, systolic and diastolic blood pressure, visual acuity, IOP, and axial length was significantly different between the two groups (Table 1). Unsurprisingly, a significant difference between the control and migraine group MIDAS score and MIDAS grade (Table 2) was documented ($p=<0.0001$).

Independent sample T tests were carried out to determine if there were any significant differences between various OCT thickness parameters (RNFL, GCL, Choroidal) in migraine patients on a non-attack

day compared to normal healthy controls. Table 3 indicates that the although the average RNFL was lower in the migraine population for several parameters, all RNFL variables did not reach statistical significance. A significant decrease in the right eye inferior parafoveal ganglion cell layer in the migraine group of patients (mean = 25.15, SD = 4.08) compared to normal healthy controls (mean = 28.81, SD = 4.85; t = (27) = 2.17, p = 0.039) was documented (Table 4). The magnitude of the differences in the means was also large, with eta squared equal to 0.15 (Fig 1). No other ganglion cell layer or choroidal thickness (Table 5) reached significance. An independent sample T test was then carried out to determine if there was a significant difference between any of the thickness parameters in the right and left eyes for migraine patients with aura versus those without. Again, all variables were found to be insignificant. Finally, a correlation was used to investigate any potential relationship between foveal ganglion cell complex in the left eye and either MIDAS score or duration of years since migraine diagnosis. No significant relationship was documented ($p > 0.05$).

Discussion

The aim of the present study was to investigate variations in RNFL, ganglion cell layer or choroidal thickness in migraine patients compared to normal healthy controls. We report that although the RNFL was thinner in the migraineurs for several parameters, current results did not reach statistical significance. Nonetheless, these findings are in line with a recent quantitative meta-analysis, consisting of 26 separate studies, that reported thinner RNFL in migraineurs when their results were compared against normal healthy controls [35]. Results from Table 3 indicates that although the RNFL was thinner in the migraineurs for several parameters, current results did not reach significance. A likely explanation for this difference is that our study did not have a sufficient sample size to detect these differences. This study highlights the importance of combining single trials like this one, into a meta- analysis in order to provide a more precise estimate. Our data is therefore presented in full to enable researchers to include this in their future analysis. Findings add further support to the hypothesis that repetitive ocular haemodynamic alterations, during migraine attacks, lead to hypoxic injury and cell death. The role of oxidative stress in migraine and its effect on treatment has already been documented [36][37]. Both cerebral [38,39] and retinal [40] vasospasm in migraine has also been highlighted. Researchers have postulated that hypoxia caused by intermittent vasospasm is a risk factor for the progression of visual field loss in normal tension glaucoma [41]. Migraine [42] and NTG [41] have a known female predominance. The increased number of females in the current migraine cohort therefore reflects the known preponderance of migraine in this specific population. The exact aetiology behind this gender difference is unknown. However, some have postulated that the higher frequency of vasospasm [43,44] and vascular disease [13] found in females, contributes towards the higher prevalence of normal tension glaucoma and migraine.

The impacts of recurring episodes of haemodynamic alterations in migraineurs, is probably not limited to the RNFL. This study also investigated any differences between either the GCL or CT in migraineurs versus normal healthy controls. Our results suggest that migraineurs have significantly reduced inferior parafoveal ganglion cell layer in their right eye, during the interictal period ($p= 0.039$). The large effect size suggests that 15% of the variance in the para foveal inferior GCL is explained by a migraine

diagnosis. Similar findings have been documented elsewhere [24–27,45] and it is of particular interest to note that several authors have record thinning, specifically within the inferior hemisphere [25–27]. Nevertheless, it is important to acknowledge that these findings have not been replicated consistently across the literature [28–30]. This highly explorative study was developed with a large number of comparisons and a small sample size. When small group sizes are employed it has been suggested that it might be necessary to adjust the alpha upwards to either 0.10 or 0.15 in order to account for insufficient numbers (Stevens 1996). When a large number of comparisons are used it is conventional to adjust the alpha level down by dividing the alpha level by the number of comparisons used. In this case the alpha would be divided by a minimum of two (for each eye examined) or a maximum of 10, if all the examined parameters were included (Table 4). When both factors are considered together this would leave a significant alpha to lie anywhere between 0.075 and 0.015. With this in mind, it suggests that current results are at best borderline and that the study would definitely benefit from repetition. Alternatively, the data could be included in a systematic review and meta-analysis investigating the GCL and CT in migraineurs, as to date none has been carried out. For this reason, all findings, including negative results have been presented to ensure that that a positive bias is not introduced into future meta-analysis. The average inferior parafoveal GCL measurements were also reduced in the left eye for the migraine population, however the figures again did not reach statistical significance. One possible explanation for this slight disparity between eyes is that the thickness is primarily reduced in the side where the headache was localised to. Unfortunately, when we looked back to this section of the questionnaire the majority of participants failed to fill in this section and we must therefore conclude that further research is necessary to investigate this hypothesis.

Twenty percent of people living with migraine report a visual illusion known as an aura preceding their headache (Russell 1996). Typical symptoms include scintillating shapes, adjacent to the central vision, expanding peripherally over 5 to 20-minute period [46]. It has been suggested that decreased visual sensitivity might be caused by localised vascular events [47]. Temporary alterations in ocular perfusion during a migraine attack could result in focal hypoxia to both the optic nerve head and the retina, resulting in transient changes to vision. We did not find any relationship between migraine with aura and migraine without aura and any of the thickness parameters.

A further aim was to examine if there is any relationship between severity and/or duration of migraine and ocular thickness. In the present study, we did not find any relationship between the two. A significant relationship between the severity and duration of migraine and the thickness of posterior ocular structures has been documented however, this study employed a significantly larger sample size [48]. Negative findings, therefore suggest that either there is no relationship between the two or that the small sample size was insufficient to detect a positive relationship. Presenting future results in full even when negative will allow future researchers to reliably investigate this variable as part of a meta-analysis.

The outcomes from this study all indicate that this area of research would greatly benefit from a systematic review and meta-analysis which is not limited to the RNFL, but also includes the GCL and the choroidal thickness of migraine patients compared to normal healthy controls. Researchers should also

determine the impact of migraine type (with or without aura) and the MIDAS score/grade. As there is some suggestion from the literature that both parameters have ocular implications which can be measured in vivo.

References

1. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for. Lancet. 2017;16: 1211–1259. doi:10.1016/S0140-6736(17)32154-2
2. Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton RB, Scher AI, et al. The global burden of headache: A documentation of headache prevalence and disability worldwide. Cephalalgia. 2007. pp. 193–210. doi:10.1111/j.1468-2982.2007.01288.x
3. World Health Organization., Lifting the Burden (Organization). Atlas of headache disorders and resources in the world 2011. World Health Organization; 2011.
4. Sacco S, Ricci S, Degan D, Carolei A. Migraine in women: the role of hormones and their impact on vascular diseases. The Journal of Headache and Pain. 2012;13: 177–189. doi:10.1007/s10194-012-0424-y
5. Steiner T, Scher A, Stewart W, Kolodner K, Liberman J, Lipton R. The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. Cephalagia. 2003;23: 519–527. doi:10.1046/j.1468-2982.2003.00568.x
6. Eadie MJ. The pathogenesis of migraine - 17th to early 20th Century understandings. Journal of Clinical Neuroscience. 2005;12: 383–388. doi:10.1016/j.jocn.2004.12.003
7. May A, Goadsby PJ. The Trigeminovascular System in Humans: Pathophysiologic Implications for Primary Headache Syndromes of the Neural Influences on the Cerebral Circulation. Journal of Cerebral Blood Flow and Metabolism. 1999;19: 115–127. doi:10.1097/00004647-199902000-00001
8. Russo A, Coppola G, Pierelli F, Parisi V, Silvestro M, Tessitore A, et al. Pain Perception and Migraine. Frontiers in Neurology. 2018;9. doi:10.3389/fneur.2018.00576
9. Goadsby PJ. The pharmacology of headache. Progress in Neurobiology. 2000;62. doi:10.1016/S0301-0082(00)00010-1
10. Carolei A, Marini C, di Napoli M, di Gianfilippo G, Santalucia P, Baldassarre M, et al. High Stroke Incidence in the Prospective Community-Based L'Aquila Registry (1994–1998). Stroke. 1997;28. doi:10.1161/01.STR.28.12.2500
11. Tzourio C, Iglesias S, Hubert JB, Visy JM, Alperovitch A, Tehindrazanarivelo A, et al. Migraine and risk of ischaemic stroke: a case-control study. BMJ. 1993;307. doi:10.1136/bmj.307.6899.289
12. Richard CR, Connor MB. Complicated migraine a study of permanent neurological and visual defects caused by migraine. The Lancet. 1962;280. doi:10.1016/S0140-6736(62)90782-1
13. Sacco S, Ornello R, Ripa P, Pistoia F, Carolei A. Migraine and Hemorrhagic Stroke. Stroke. 2013;44. doi:10.1161/STROKEAHA.113.002465

14. Sacco S, Ripa P, Grassi D, Pistoia F, Ornello R, Carolei A, et al. Peripheral vascular dysfunction in migraine: a review. The Journal of Headache and Pain. 2013;14: 80. doi:10.1186/1129-2377-14-80
15. Tripathi S, Ariga M, Srinivasan M. Review article: Ocular blood flow in glaucoma. TNOA Journal of Ophthalmic Science and Research. 2020;58: 180. doi:10.4103/tjosr.tjosr_81_20
16. Flammer J, Orgül S, Costa VP, Orzalesi N, Krieglstein GK, Serra LM, et al. The impact of ocular blood flow in glaucoma. Progress in Retinal and Eye Research. 2002;21: 359–393. doi:10.1016/S1350-9462(02)00008-3
17. KILLER HE, FORRER A, FLAMMER J. Retinal Vasospasm During an Attack of Migraine. RETINA. 2003;23: 253–254. doi:10.1097/00006982-200304000-00023
18. Beversdorf D, Stommel E, Allen C n, Stevens R, Lessell S. Recurrent Branch Retinal Infarcts in Association With Migraine. Headache: The Journal of Head and Face Pain. 1997;37: 396–399. doi:10.1046/j.1526-4610.1997.3706396.x
19. Agostoni E, Rigamonti A. Migraine and small vessel diseases. Neurological Sciences. 2012;33: 51–54. doi:10.1007/s10072-012-1041-x
20. Ascaso FJ, Marco S, Mateo J, Martínez M, Esteban O, Grzybowski A. Optical Coherence Tomography in Patients with Chronic Migraine: Literature Review and Update. Frontiers in Neurology. 2017;8. doi:10.3389/fneur.2017.00684
21. Lin X, Yi Z, Zhang X, Liu Q, Cai R, Chen C, et al. Retinal nerve fiber layer changes in migraine. Medicine. 2020;99. doi:10.1097/MD.0000000000021680
22. Zengin MO, Elmas Z, Cinar E, Kucukerdonmez C. Choroidal thickness changes in patients with migraine. Acta Neurologica Belgica. 2015;115. doi:10.1007/s13760-014-0301-3
23. Colak HN, Kantarci FA, Tatar MG, Eryilmaz M, Uslu H, Goker H, et al. Retinal nerve fiber layer, ganglion cell complex, and choroidal thicknesses in migraine. Arquivos Brasileiros de Oftalmologia. 2015;79: 78–81. doi:10.5935/0004-2749.20160024
24. Reggio E, Chisari CG, Ferrigno G, Patti F, Donzuso G, Sciacca G, et al. Migraine causes retinal and choroidal structural changes: evaluation with ocular coherence tomography. Journal of Neurology. 2017;264. doi:10.1007/s00415-016-8364-0
25. Kanar HS, Toz HT, Penbe A. Comparison of retinal nerve fiber layer, macular ganglion cell complex and choroidal thickness in patients with migraine with and without aura by using optical coherence tomography. Photodiagnosis and Photodynamic Therapy. 2021;34. doi:10.1016/j.pdpdt.2021.102323
26. Ekinci M, Ceylan E, Çağatay HH, Keleş S, Hüseyinoğlu N, Tanyıldız B, et al. Retinal nerve fibre layer, ganglion cell layer and choroid thinning in migraine with aura. BMC Ophthalmology. 2014;14. doi:10.1186/1471-2415-14-75
27. Abdellatif MK, Fouad MM. Effect of duration and severity of migraine on retinal nerve fiber layer, ganglion cell layer, and choroidal thickness. European Journal of Ophthalmology. 2018;28: 714–721. doi:10.1177/1120672117750054

28. Yülek F, Dirik EB, Eren Y, Simavlı H, Uğurlu N, Çağıl N, et al. Macula and Retinal Nerve Fiber Layer in Migraine Patients: Analysis By Spectral Domain Optic Coherence Tomography. Seminars in Ophthalmology. 2015;30. doi:10.3109/08820538.2013.833270
29. Yener AÜ, Korucu O. Quantitative analysis of the retinal nerve fiber layer, ganglion cell layer and optic disc parameters by the swept source optical coherence tomography in patients with migraine and patients with tension-type headache. Acta Neurologica Belgica. 2019;119: 541–548. doi:10.1007/s13760-018-1041-6
30. Acer S, O uzhano lu A, Çetin EN, Ongun N, Pekel G, Kaşikçi A, et al. Ocular pulse amplitude and retina nerve fiber layer thickness in migraine patients without aura. BMC Ophthalmology. 2016;16. doi:10.1186/s12886-015-0180-2
31. Olesen J. The International Classification of Headache Disorders. Headache: The Journal of Head and Face Pain. 2008;48. doi:10.1111/j.1526-4610.2008.01121.x
32. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38: 1–211. doi:10.1177/0333102417738202
33. Tan CS, Ouyang Y, Ruiz H, Sadda SR. Diurnal Variation of Choroidal Thickness in Normal, Healthy Subjects Measured by Spectral Domain Optical Coherence Tomography. Investigative Opthalmology & Visual Science. 2012;53. doi:10.1167/iovs.11-8782
34. Yamashita T, Yamashita T, Shirasawa M, Arimura N, Terasaki H, Sakamoto T. Repeatability and Reproducibility of Subfoveal Choroidal Thickness in Normal Eyes of Japanese Using Different SD-OCT Devices. Investigative Opthalmology & Visual Science. 2012;53. doi:10.1167/iovs.11-8836
35. Lin X, Yi Z, Zhang X, Liu Q, Zhang H, Cai R, et al. Retinal nerve fiber layer changes in migraine: a systematic review and meta-analysis. Neurol Sci. 2021;42: 871–881. doi:10.1007/s10072-020-04992-4/Published
36. Bulboacă AE, Stănescu IC, Bolboacă SD, Bulboacă AC, Bodizs GI, Nicula CA. Retinal Nerve Fiber Layer Thickness and Oxidative Stress Parameters in Migraine Patients without Aura: A Pilot Study. Antioxidants. 2020;9. doi:10.3390/antiox9060494
37. Tripathi GM, Kalita J, Misra UK. A study of oxidative stress in migraine with special reference to prophylactic therapy. International Journal of Neuroscience. 2018;128. doi:10.1080/00207454.2017.1374959
38. Vinciguerra L, Cantone M, Lanza G, Bramanti A, Santalucia P, Puglisi V, et al. Migrainous infarction and cerebral vasospasm: Case report and literature review. Journal of Pain Research. 2019;12: 2941–2950. doi:10.2147/JPR.S209485
39. Boasso LE, Fischer AQ. Cerebral Vasospasm in Childhood Migraine During the Intermigrainous Period. Journal of Neuroimaging. 2004;14. doi:10.1111/j.1552-6569.2004.tb00233.x
40. Killer HE, Forrer A, Flammer J. Retinal Vasospasm During an Attack of Migraine. Retina The Journal of Retinal and Vitreous Diseases . 2003;23: 253–254. doi:10.1097/00006982-200304000-00023

41. Drance S, Anderson DR, Schulzer M. Risk factors for progression of visual field abnormalities in normal-tension glaucoma. American Journal of Ophthalmology. 2001;131. doi:10.1016/S0002-9394(01)00964-3
42. Stewart WF, Wood C, Reed ML, Roy J, Lipton RB. Cumulative lifetime migraine incidence in women and men. Cephalalgia. 2008;28: 1170–1178. doi:10.1111/j.1468-2982.2008.01666.x
43. Gramer G, Weber BHF, Gramer E. Migraine and Vasospasm in Glaucoma: Age-Related Evaluation of 2027 Patients With Glaucoma or Ocular Hypertension. Investigative Opthalmology & Visual Science. 2015;56. doi:10.1167/iovs.15-17274
44. Gasser P, Flammer J. Blood-Cell Velocity in the Nailfold Capillaries of Patients with Normal-Tension and High-Tension Glaucoma. American Journal of Ophthalmology. 1991;111. doi:10.1016/S0002-9394(14)73703-1
45. Gunes A, Karadag AS, Yazgan S, Celik HU, Simsek A. Evaluation of retinal nerve fibre layer, ganglion cell layer and choroidal thickness with optical coherence tomography in migraine patients: a case-control study. Clinical and Experimental Optometry. 2018;101. doi:10.1111/cxo.12585
46. Hadjikhani N, Sanchez Del Rio M, Wu O, Schwartz D, Bakker D, Fischl B, et al. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. PNAS April. 2001. Available: www.pnas.orgcgidoi10.1073pnas.071582498
47. Flammer J, Pache M, Resink T. Vasospasm, its Role in the Pathogenesis of Diseases with Particular Reference to the Eye. Prog Retin Eye Res. 2001;20: 319–49. doi:10.1016/s1350-9462(00)00028-8
48. Abdellatif MK, Fouad MM. Effect of duration and severity of migraine on retinal nerve fiber layer, ganglion cell layer, and choroidal thickness. European Journal of Ophthalmology. 2018;28: 714–721. doi:10.1177/1120672117750054

Tables

Table 1. Demographics of study participants shows that there were no statistically significant differences between the control and the migraine group in age, gender, systolic and diastolic blood pressure.

	Migraine (n=13)	Control group (n=16)	p Value
Age (years) **Mean (SD)** **min - max**	 28 (8.79) 18 - 45	 26.6 (6.89) 19 - 43	 0.846
Gender	12 females; 1 male	9 females; 7 males	0.101
SBP (mm Hg) **Mean (SD)** **min - max**	 116.39 (12.01) 95 -138	 122.75 (16.27) 100 -162	 0.251
DBP (mm Hg) **Mean (SD)** **min - max**	 79.15 (10.74) 59 - 99	 77.31 (8.58) 57 - 91	 0.612
MIDAS Score **Mean (SD)** **min - max**	 **27 (28.4)** **1 - 84**	 **0.06 (0.25)** **0 - 1**	 **<0.0001**
MIDAS Grade **Mean (SD)** **Min-max**	 **2.62 (1.33)** **1-4**	 **0 (0)** **0-0**	 **<0.0001**

Table 2. Ocular characteristics of the study participants shows that there were no statistically significant differences between the control and the migraine group in visual acuity, IOP, CCT or axial length. * indicates non-parametric analysis carried out.

	Migraine (n=13)	Control group (n=16)	p Value
Visual Acuity right eye (logMar) Mean (SD)	-0.02 (0.07)	-0.07 (0.09)	0.125
Visual Acuity left eye (logMar) Mean (SD)	-0.04 (0.08)	-0.07 (0.12)	0.577
IOP right eye (mm Hg) Mean (SD)	13.46 (2.02)	12.94 (2.57)	0.423*
IOP left eye (mm Hg) Mean (SD)	13.38 (1.94)	13.13 (1.86)	0.589*
CCT right eye (µm) Mean (SD) min - max	505.62 (27.53)	512.50 (39.22)	0.598
CCT left eye (µm) Mean (SD)	501.31 (26.41)	510.38 (37.90)	0.472
Axial length right eye (mm) Mean (SD)	23.69 (1.22)	24.09 (1.34)	0.418
Axial length left eye (mm) Mean (SD)	23.60 (1.23)	23.96 (1.32)	0.451

Table 3: Showing the difference RNFL thickness in both eyes, between the migraineurs and normal healthy controls (right eye = RE; Left eye =LE).* Non-parametric analysis carried out.

	Migraine (n=13)	Control group (n=16)	p Value
Average RNFL RE	*103.46 (17.28)*	*105.56 (10.08)*	0.559*
Average RNFL LE	*103.54 (17.00)*	*105.25 (11.48)*	0.531*
Temporal RNFL RE	76.46 (12.45)	76.94 (10.67)	0.913
Temporal RNFL LE	73 (10.58)	72.56 (9.81)	0.909
Superior RNFL RE	*126.23 (27.40)*	*128.63 (21.10)*	0.792
Superior RNFL LE	*127.46 (26.76)*	*129.69 (21.25)*	0.805
Inferior RNFL RE	135.38 (24.11)	135.25 (16.97)	0.986
Inferior RNFL LE	138.69 (23.67)	137.56 (18.38)	0.886
Nasal RNFL RE	*76.00 (17.73)*	*81.94 (15.23)*	0.340
Nasal RNFL LE	*75.38 (14.28)*	*81.31 (16.67)*	0.319

Table 4: Showing the difference GCL thickness in both eyes, between the migraineurs and normal healthy controls (right eye = RE; Left eye =LE).* Non-parametric analysis carried out.

	Migraine (n=13)	Control group (n=16)	p Value
Central fovea GCL RE	4.31 (1.38)	4.31 (1.66)	0.948
Central fovea GCL LE	4.15 (1.35)	4.63 (1.82)	0.329*
Parafovea temporal GCL RE	20.54 (1.76)	21.13 (1.63)	0.360
Parafovea temporal GCL LE	20.69 (2.90)	19.75 (1.65)	0.092*
Parafovea superior GCL RE	31.08 (4.94)	28.88 (2.45)	0.308*
Parafovea superior GCL LE	29.85 (2.82)	28.38 (2.09)	0.119
Parafovea inferior GCL RE	***25.15 (4.08)***	*28.81 (4.85)*	***0.039***
Parafovea inferior GCL LE	*26.85 (3.18)*	*27.19 (3.25)*	0.341
Parafovea nasal GCL RE	25.23 (2.52)	25.50 (2.22)	0.812*
Parafovea nasal GCL LE	27.47 (7.89)	25.38 (2.96)	0.846*

Table 5: Showing the difference in choroidal thickness in both eyes, between the migraineurs and normal healthy controls (right eye = RE; Left eye =LE).

	Migraine (n=13)	Control group (n=16)	p Value
Temporal choroid RE	339.46 (76.80)	328.75 (70.35)	0.699
Temporal choroid LE	323.69 (71.12)	314.63 (67.67)	0.728
Superior choroid RE	334.92 (62.19)	333.19 (57.18)	0.938
Superior choroid LE	333.62 (62.22)	312.63 (66.28)	0.391
Inferior choroid RE	325.23 (50.60)	320.69 (67.48)	0.842
Inferior choroid LE	320.38 (67.09)	312.81 (67.12)	0.765
Nasal choroid RE	319.15 (77.43)	313.25 (73.23)	0.835
Nasal choroid LE	312.38 (49.72)	324.56 (82.75)	0.645

Declarations

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Conflict of Interest:

I can confirm that there is no conflict of interests to report.

Author Contribution:

Miriam L Conway- designed the study, collected the date, analysed the data, study write up

Irene Ctori-designed the study, contributed to the write up

Figures

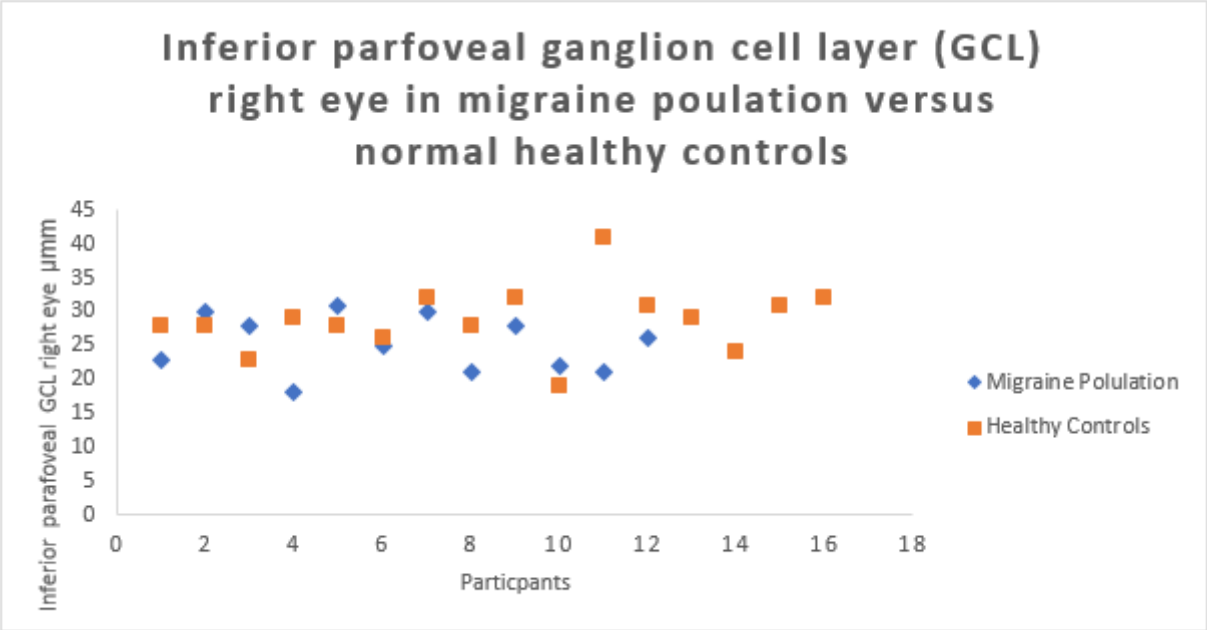

Figure 1

Showing the difference in parafoveal GCL thickness in the right eyes between the migraineurs and normal healthy controls.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ParticipantsQuestionnairev0.docx