536 Retinal Abnormalities and Neuropathology
Thursday, May 11, 2017 11:30 AM–1:15 PM
Room 324 Paper Session
Program #/Board # Range: 5641–5647
Organizing Section: Eye Movements/Strabismus/Amblyopia/ Neuro-Ophthalmology

Program Number: 5641
Presentation Time: 11:30 AM–11:45 AM
Evolution of Retinal Deformations Due to Acute NAION: Biomechanical Changes Not Related to Increased Pressure in the Neural Canal Region
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Purpose: Optic nerve head (ONH) swelling due to non-arteritic anterior ischemic optic neuropathy (NAION) spreads edema into the peripapillary retina that can extend into the macula. The induced retinal deformations, we previously described with papilledema, have not been studied in NAION. We hypothesized these folds, which are related to stresses and strains in the region of the neural canal, would have features different from those in papilledema reflecting different biomechanical processes or forces.
Methods: We prospectively studied eyes with NAION, within 2 weeks of vision loss and at 1-2 months, with perimetry and spectral domain OCT (SDOCT) images of the optic disc and macula. NAION eyes were evaluated for deformations including peripapillary fluid (PPF), peripapillary wrinkles (PPW), retinal folds (RF), choroidal folds (CF), and peripapillary creases using transaxial and *en face* views. Deformations were evaluated in relation to the retinal nerve fiber layer (RNFL) thickness, visual acuity and mean deviation (MD).
Results: At presentation, 50 study eyes had mean RNFL of 223 ± 75 μm, 37 (74%) had PPF, 28 (56%) had PPW, 21 (42%) had RF (all which were concentric), 8 (16%) had creases, and 0 had CF or vitreal traction on the optic disc. Folds or fluid affected the macula in 9 (18%) eyes. Visual acuity or MD did not correlate with having any type of fold. The RNFL was thicker in eyes with PPF ($p = 0.001$), PPW ($p=0.001$), RF ($p=0.01$) and macula involvement ($p=0.002$). At 1-2 months of the 39 eyes (mean RNFL of 112 ± 40 μm), and PPF (82%), PPW (90%), RF (87%), edema/folds in the macula (100%), and creases (82%) were absent; none of which had impact on the visual acuity or MD.
Conclusions: Retinal deformations in NAION reflect dynamic processes due to local tissue distortion and extracellular fluid. The lack of CF and radial RF, which occur with papilledema, suggests the peripapillary ONH region is not under significant pressure. All folds in NAION rapidly resolve as ONH swelling lessens and axons are lost, in contrast to papilledema where the intracranial hypertension induced pressure effect on the neural canal and folds persist despite less ONH swelling.
Commercial Relationships: Mark J. Kupersmith; **Patrick A. Sibony**, None

Program Number: 5642
Presentation Time: 11:45 AM–12:00 PM
A comparison of optic neuritis and NAION with OCT and OCT angiography
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Purpose: Nonarteritic anterior ischemic optic neuropathy (NAION) and optic neuritis are the two most common acute optic neuropathies. OCT angiography is a new tool that can evaluate the density of the radial peripapillary capillary network, which has been shown to be decreased in various chronic optic neuropathies. The goal of this study was to evaluate OCT and OCT angiography's ability to differentiate optic neuritis and NAION, and predict visual outcomes.
Methods: We performed a cross-sectional, observational study of patients with unilateral optic neuritis or NAION who presented between 2015 and 2016. Patients were included if they had unilateral optic neuritis or NAION and had OCT (Cirrus) and OCT angiography (Optovue) done at least 3 months after onset. Because a normative database for OCT angiography has not been established, we used the inter-eye difference as an approximation of change. The retinal nerve fiber layer (RNFL) and peripapillary vessel density were compared between optic neuritis and NAION using paired t test. The correlation between OCT parameters and visual outcome [Humphrey visual field mean deviation (MD)] was evaluated with Pearson correlation (R).
Results: A total of 27 patients were included(11 NAION and 16 optic neuritis). The peripapillary vessel density was more affected in NAION compared to optic neuritis, which showed an average inter-eye difference of 11.4 and 6.9 respectively ($p=0.02$), while the RNFL was equally affected in the two groups with an average difference of 23.4 and 22.3 respectively ($p=0.46$). The ratio RNFL/ MD differentiated the two groups the best where optic neuritis had an average ratio of 17.9 while NAION had an average ratio of 1.9 ($p<0.001$).
The overall inter-eye difference in the peripapillary vessel density was correlated with MD ($R=0.72$, $p<0.001$) while the RNFL was not correlated ($R= 0.25$, $p=0.22$). In the NAION group, the peripapillary vessel density and RNFL were both correlated with MD with a R of 0.80 ($p=0.003$) and 0.63 ($p=0.04$) respectively. In the optic neuritis group, the peripapillary vessel density was correlated with MD ($R= 0.62$, $p=0.02$), while the RNFL was not correlated ($R=0.12$, $p=0.68$).
Conclusions: Thinning of the RNFL in the setting of preserved visual fields is the most sensitive parameter in differentiating optic neuritis and NAION. The peripapillary vessel density on OCT angiography may better predict visual outcomes, especially in patients with optic neuritis.
Commercial Relationships: John J. Chen, None; **Jacqueline Leavitt**, None; **Jackson Abou Chehade**, None; **Raymond Iezzi**, None; **David Hodge**, None; **Randy Kardon**, None

Program Number: 5643
Presentation Time: 12:00 PM–12:15 PM
Can grading foveal hypoplasia in infants using handheld optical coherence tomography predict future visual acuity? A longitudinal cohort study
Sohaib R. Rufai[1], Mervyn G. Thomas[1], Helena Lee[2], Frank A. Proudlock[1], Irene Gottlob[1]. [1]Ulverscroft Eye Unit, University of Leicester, Kettering, United Kingdom; [2]Clinical and Experimental Sciences, University of Southampton, Southampton, United Kingdom.
Purpose: Handheld spectral-domain optical coherence tomography (HH-OCT) can be used to diagnose foveal hypoplasia in infants. However, it unclear whether HH-OCT can predict future visual acuity in infants with foveal hypoplasia. We performed a longitudinal cohort study to assess whether grading foveal hypoplasia can predict future visual acuity in patients with infantile nystagmus.
Methods: We recruited patients with infantile nystagmus aged between 6 and 24 months at the time of their first HH-OCT and graded their initial scans. Foveal tomograms were graded using the

Thomas et al grading system for foveal hypoplasia: Grade 1: shallow foveal pit, presence of outer nuclear layer (ONL) widening, presence of outer segment (OS) lengthening; Grade 2: Grade 1 but absence of foveal pit; Grade 3: Grade 2 but absence of OS lengthening; Grade 4: Grade 3 but absence of ONL widening; atypical foveal hypoplasia: shallow foveal pit, disruption of the inner segment ellipsoid band. Patients were followed up 19.61 to 52.89 (mean: 39.78, S.D. 8.70) months later when they could reliably co-operate with logMAR visual acuity measured with Glasgow and/or Cardiff Acuity Cards. Data was analysed using a linear mixed regression model including both foveal hypoplasia grading, eye recorded and age at testing (both OCT imaging and visual acuity) in the model.

Results: We imaged 38 eyes from 19 patients with infantile nystagmus aged between 7.16 and 23.90 (mean: 12.45, S.D. 4.79) months at the time of their first HH-OCT. This patient cohort included albinism (n=12), idiopathic infantile nystagmus (IIN) (n=6) and achromatopsia (n=1). Foveal hypoplasia was identified in 31 eyes which included Grade 1 (n=19), Grade 2 (n=0), Grade 3 (n=4), Grade 4 (n=6) and atypical foveal hypoplasia (n=2). Normal tomograms were seen in seven eyes. Foveal hypoplasia grading was a strong predictor of visual acuity later in life ($p<0.001$; $F=59.3$; $\beta=0.19$, 95% CI = 0.14 to 0.24).

Conclusions: Our findings demonstrate a strong correlation between the severity of foveal hypoplasia using our grading system in infancy with visual acuity at a later age when reliable. HH-OCT has the potential to predict future visual acuity in infants with foveal hypoplasia.

Commercial Relationships: Sohaib R. Rufai, Spectrum (R), Bayer (R); **Mervyn G. Thomas**, None; **Helena Lee**, None; **Frank A. Proudlock**, None; **Irene Gottlob**, None

Program Number: 5644
Presentation Time: 12:15 PM–12:30 PM

Hemispheric analysis for detecting intraretinal thickness alterations in mild cognitive impairment and Alzheimer's disease

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Purpose: Detail analysis of tomographic thicknesses of intraretinal layers may provide more sensitive detection of neurodegeneration in mild cognitive impairment (MCI) and Alzheimer's disease (AD). Our study was to evaluate hemispheric intraretinal thickness maps in MCI and AD and their diagnostic values compared to conventional ganglion cell layer thickness analysis.

Methods: Totally 29 patients diagnosed with AD (n=12) and MCI (n=17) and 22 age matched controls were recruited. All subjects were imaged with custom ultrahigh-resolution OCT (URH-OCT) to obtain 6 intraretinal thickness maps and Zeiss Cirrus HD-OCT for obtaining ganglion cell-inner plexiform layer (GCIPL) thickness map. Orion software was used and further analysis was done using hemispheric partition and the Early Treatment Diabetic Retinopathy Study (ETDRS) methods. Receiver operating characteristic curves were calculated and sensitivity and specificity were used to evaluate diagnostic performance.

Results: Using hemispheric partition, the retinal nerve fiber layer (RNFL) thickness of nasal inferior, inner temporal superior (ITS), inner temporal inferior (ITI), inner nasal inferior (INI) and outer nasal inferior sectors and the inner nuclear layer (INL) thickness of nasal superior, ITS, ITI and INI sectors were significantly thinner in the AD than control ($p<0.05$). The GCIPL thickness of superior, ITS, ITI, INI and outer nasal superior (ONS) sectors in the AD were significantly thinner than control ($p<0.05$). In contrast, only GCIPL thickness of superior, ITS, ITI, INI, ONS and inner nasal superior area in the MCI were significantly thinner than control (All $p<0.05$). Using EDTRS partition, GCIPL thickness of the inner superior sector in MCI was significant thinner than control ($p<0.05$). Interestingly, GCIPL analysis by the conventional method only found a significant thinning located at inferior temporal sector ($p<0.05$). The best distinguishing parameter was the ITS thickness of INL (0.76; 95% confidence interval [CI]=0.59–0.92) for AD patients and the ONS thickness of GCIPL by UHR-OCT for MCI (0.81; 95% CI=0.63–0.99).

Conclusions: The thinning of the RNFL, GCIPL and INL can be detected by the hemispheric method using UHR-OCT in the AD and MCI patients, which appeared to be more sensitive for early detection of retinal neurodegeneration than the EDTRS partition and conventional GCIPL analysis.

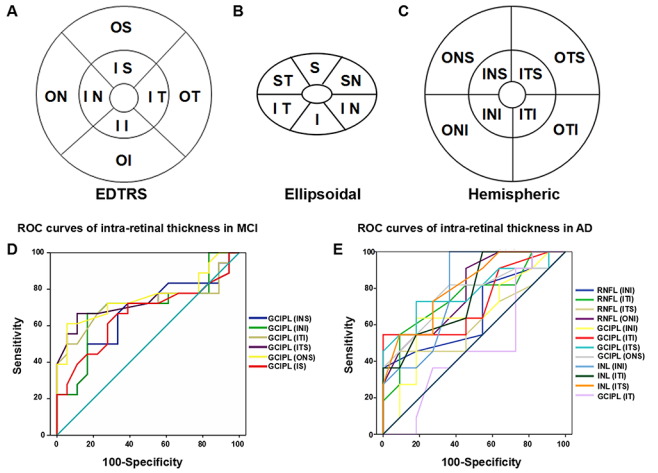

Fig. 1 Representation of ROC curves obtained with the retinal RNFL, GCIPL, INL thickness parameters in MCI and AD provided by the UHR-OCT and Zeiss OCT device. Two zoning systems were used to define sectors of intraretinal layers for calculating thickness. Three concentric rings including 1, 3, and 6 mm diameters were used to divide the map into nine zones. The central 1 mm zone of the fovea was removed.The inner and outer annuli were then divided into four quadrants for each annulus. In the ETDRS definition, the quadrantal division was done using 45° and 135° medians (Left, A). In the hemispheric definition, the division was done using vertical and horizontal medians (Right, C). The software detects and measures the GCIPL thicknesses automatically within a 14.13 mm² elliptical annulus area centered on the fovea from 3-dimensionals by Zeiss OCT. The annulus has an inner vertical diameter of 1mm and an outer diameter of 4mm, and an inner horizontal diameter of 1.2mm and an outer diameter of 4.8mm. (Middle, B). (D) Representation of ROC curves obtained with the thickness of the RNFL, GCIPL and INL in MCI provided by the UHR-OCT device. The largest areas under the ROC curves were for ONS thickness of GCIPL (0.81; 95% confidence interval [CI], 0.63–0.99); (E) Representation of ROC curves obtained with the thickness of RNFL, GCIPL and INL by the UHR-OCT device and the thickness of GCIPL by Zeiss OCT in AD. The largest areas under the ROC curves were for the ITS thickness of INL (0.76; 95% confidence interval [CI], 0.59–0.92).

Commercial Relationships: Yi Shao; **Hong Jiang**, None; **Yantao Wei**, None; **Yingying Shi**, None; **Clinton Wright**, None; **Xiaoyan Sun**, None; **Byron L. Lam**, None; **Tatjana Rundek**, None; **Jianhua Wang**, None

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Program Number: 5645
Presentation Time: 12:30 PM–12:45 PM

Total macular thickness correlates with parietal cortical atrophy on MRI in early onset Alzheimer's disease

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Purpose: As a protrusion from the brain, the retina might serve as a patient-friendly source of biomarkers reflecting neurodegeneration. Previous research showed thinning of total macular and peripapillary retinal nerve fiber layer (RNFL) thickness measured with OCT

in patients with Alzheimer's Disease (AD) compared to controls. This observational pilot aimed to i. determine retinal thickness with Spectral Domain OCT (SD-OCT) in amyloid positive, early onset AD (EOAD) patients and controls, and ii. to correlate retinal thickness to cortical atrophy scores on MRI as established AD biomarkers.
Methods: Fifteen subjects with AD and 15 controls from the Amsterdam Dementia Cohort (age<70y, Mini-Mental State Examination(MMSE)>16) were included. All patients met NIA-AA criteria and were amyloid positive in CSF and/or on amyloid-PET. Controls were amyloid negative subjects with subjective cognitive decline (SCD). Subjects underwent a complete ophthalmological and neurological examination including MRI and SD-OCT of the macula and optic disk (Heidelberg, Spectralis). Patients were excluded for glaucoma. Peripapillary RNFL and total macular thickness were measured and correlated with visual cortical atrophy scores on MRI: medial temporal lobe atrophy (MTA), global cortical atrophy (GCA) and parietal cortical atrophy (PCA).
Results: Peripapillary RNFL thickness was 95.9µm±9.0 for AD patients versus 97.5µm±6.96 for controls (t-test, p=0.575). Total macular thickness (mean of inner ring and outer ring of ETDRS grid) was 316.1µm±11.0 for AD patients versus 320.5µm±7.5 for controls (t-test, p=0.216). Total macular thickness was significantly correlated (after Bonferroni, α<0.017) with PCA (Spearman's rho= -0.603, p=0.001) but not with GCA (Spearman's rho= -0.443, p=0.018) and MTA (Spearman's rho= -0.286, p=0.140) in the total study group(figure 1).
Conclusions: Peripapillary RNFL and total macular thickness were not significantly decreased in an amyloid positive EOAD cohort without glaucoma compared to controls. Total macular thickness was significantly correlated to PCA on MRI, supporting the hypothesis that neurodegenerative diseases may be reflected by retinal changes. Future research in larger cohorts with established AD biomarkers are needed to asses the diagnostic value of retinal thickness for AD diagnosis.

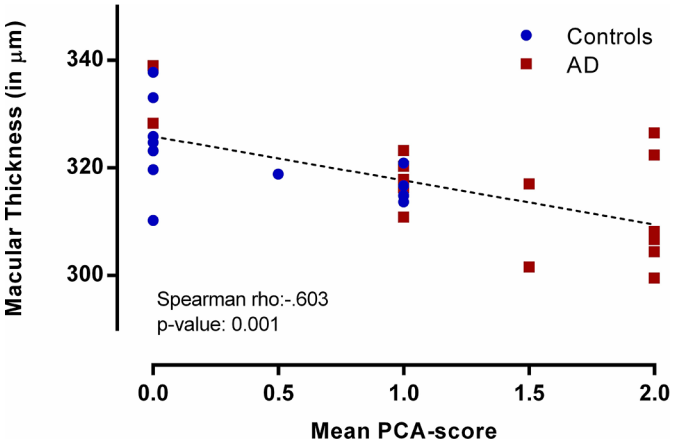

Figure 1: Macular thickness is correlated with parietal cortical atrophy
Commercial Relationships: Jurre den Haan, None; **SF Janssen**, None; **JA van de Kreeke**, None; **P Scheltens**, None; **FH Bouwman**, None; **Frank Verbraak**, None

Program Number: 5646
Presentation Time: 12:45 PM–1:00 PM
Evaluation of Retinal Layers in Patients with Multiple Sclerosis or Neuromyelitis Optica Spectrum Disease Using ERG Oscillatory Potentials, mfERG and OCT
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Purpose: To determine oscillatory potentials (OP) on full-field ERG, multifocal (mf) ERG and retinal layer thickness measurements using spectral domain-optical coherence tomography (sd-OCT) in patients with multiple sclerosis (MS) and neuromyelitis optica (NMO) and NMO spectrum (NMOsp) disease.
Methods: 167 eyes of 89 subjects divided in groups: MS with (MSON) and without (MSnon-ON) previous ON, NMO, and NMOsp without ON (NMO non-ON) (with extensive transverse myelitis) and controls were evaluated. Subjects were submitted to ERG OP determination and mf-ERG amplitude measurements using the RETI System®. For mfERG a 61-hexagon stimulus pattern was presented on a pseudo randomic form on a 21-inch black-and-white flat monitor. Mf-ERG P1 and N2 responses, were grouped in 2 concentric rings after excluding the outermost ring responses. Subjects underwent macular Spectralis-OCT scanning. Full-thickness macular and 6 segmented layers: retinal nerve fiber layer (RNFL), Ganglion Cells Layer (GCL), Inner Plexiform Layer (IPL), Inner Nuclear Layer, Outer Plexiform Layer and Outer Nuclear Layer were determined. Measurements were compared using generalized estimating equation models.
Results: Average macular GCL and IPL were significantly thinner than controls for all patient groups (p<0.05). Compared to controls full thickness macular measurements was significantly reduced in MSON and NMO eyes while macular RNFL was reduced in all but the NMOsp non-ON groups. No significant difference was observed in the remaining layers. Mean±SD average OP was increased in NMO eyes compared to controls (18.5±5.5 and 15.1±8.7, respectively, p<0.05) and did not differ in the other groups. Significant higher average P1 and N2 amplitude values were observed for total, central and peripheral ring mfERG determinations in both MS groups compared to controls (p<0.05). No significant difference was observed for NMO and NMOsp non-ON groups compared to controls except for increased total (both groups) and peripheral (NMO group) P1 amplitude response.
Conclusions: While MS and NMO leads to predominant abnormalities in inner retinal layers on sd-OCT, ERG findings indicate dysfunction also in outer retinal function. Combined to sd-OCT, ERG and mfERG could be useful in the differentiation of MS and NMO but further studies are necessary to better understand such findings.
Commercial Relationships: Thiago G. Filgueiras; **Maria Kiyoko Oyamada**, None; **Rony C. Preti**, None; **Samira A. Pereira**, None; **Dagoberto Calegaro**, None; **Mario R. Monteiro**, None
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Presentation Time: 1:00 PM–1:15 PM
Retinal abnormalities in patients with different severities of traumatic brain injury
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Purpose: Recent studies report varying degrees of structural and functional abnormalities in the inner retina of traumatic brain injury

(TBI) patients. The extent to which such abnormalities are related to the severity of injury is less well known. We sought to quantify inner retinal abnormalities in mild versus severe civilian TBI patients and their relation to functional abnormalities of the central visual pathway.

Methods: Volume scans of the macula and optic nerve head were acquired with spectral domain optical coherence tomography in both eyes of 12 patients with mild TBI and 19 patients with severe TBI, 10 of 19 were with homonymous hemianopia (HH) (time post-injury: 0.25–9.4 years). Severity was assessed using the Glasgow Coma Scale or a characterization of neuroimaging results. Peripapillary retinal nerve fiber layer thickness (RNFLT) and macular ganglion cell-inner plexiform layer thickness (GCIPLT) were quantified globally and in sectors, and compared with instrument-based normative data. Photopic negative response (PhNR) amplitudes were measured in 20 of these patients using the full-field flash electroretinogram and compared to normative data. Mean deviation (MD) was quantified via 30-2 standard automated perimetry.

Results: Global or sectoral GCIPLT and RNFLT, MD and PhNR amplitude were abnormal in 50%, 47%, 65% and 65% of all eyes, respectively. Global GCIPL was thinner in a greater percentage of severe versus mild TBI patients (68% vs. 0%, $P<.05$; χ^2 test). Within the severe TBI group, eyes with HH had thinner global GCIPLs more frequently than in non-HH patients (73% vs. 55%, $P<.05$; χ^2 test). Within the mild TBI group, 5 of 8 patients had reduced PhNR amplitudes while none had global structural damage. A significant relationship between MD and global GCIPLT ($P<.05$; Spearman's rank correlation) was found across all eyes ($r=0.53$) and within severe patients ($r=0.6$), suggesting that eyes with more extensive field loss tended to have greater thinning of inner retinal structures.

Conclusions: There was a higher prevalence of structural damage in the inner retina in severe TBI versus mild TBI patients. Severe TBI patients with HH had the highest frequency of structural damage among all groups. PhNR measurement may detect functional abnormalities in the inner retina in mild TBI patients without structural damage. Inner retinal measures may serve as objective biomarkers to better classify and diagnose TBI.

Commercial Relationships: Jakaria Mostafa, None; **Suzanne Wickum**, None; **Laura J. Frishman**, None; **Jason Porter**, None

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