Multiple Sclerosis (MS) is a demyelinating disease of the nervous system. In this longitudinal study 177 MS patients underwent spectral domain optical coherence tomography (SD-OCT) scanning and clinical assessment at baseline and after two years of follow up. Clinical assessment consisted of history of MS, Expanded Disability Status Scale (EDSS), symbol digit modalities test (SDMT), 9-hole peg test (9-HPT) and timed 25-foot walk test (T25-FWT). The macular GCPl and peripapillary RNFL thicknesses were quantified. Generalised estimating equations and linear regression analyses were used to assess longitudinal changes in IRL thicknesses and to test the relationship between baseline OCT and clinical measurements.

Results: Patients had a mean disease duration of 20.5 years (± 7.0) at baseline and 67.8% (120/177) was female. Thirty-five patients (19.8%) had a history of bilateral MS, 58 patients (32.8%) had a history of unilateral MS and 84 patients (47.5%) never experienced an episode of MSON (MSNON). Overall, patients showed significant thinning of the GCPl (0.26 µm/year [95% CI 0.19 – 0.33, p < 0.001]) and the RNFL (0.33 µm/year [95%CI (0.22 – 0.44), p < 0.001]). There was no difference in atrophy rate between MSNON and MSNON eyes (GCPl p = 0.470, RNFL p = 0.387). No association was found between changes in IRL thickness and changes in test scores on the SDMT, 9-HPT or T25 -FWT. Likewise, patients who had progressed on the EDSS did not show more atrophy over time compared to those who did not (GCPl p = 0.391, RNFL p = 0.414).

Conclusions: The data suggest that IRL atrophy is a robust measure for progressive neurodegeneration in MS even in the clinical context of a previous episode of MSNON. Evidence for progressive atrophy in the visual system could however not be related to disability progression of broader cognitive and physical function.

Commercial Relationships: Danko Coric, None; Jenny Nij Bijvank, None; Joep Killestein, None; Bernard Uitdehaag, None; Axel Petzold, None; Lisanne Balk, TEVA (F)
Purpose: To test the relationship between saccadic parameters and cognitive function, taking age, gender and visual acuity into account as possible confounders.

Results: Of all 51 patients, 17 were classified as MCI and 11 as SCI. Table 1 summarises the patient characteristics. The subgroup with a lower gain (hystermetric saccades) and a lower peak velocity in the pro-saccade task, had significantly higher odds for being SCI. Logistic regression was used to test the relationship between saccadic parameters and cognitive function, taking age, gender and visual acuity into account as possible confounders.

Conclusions: Cognitive function in MS was related to peak velocity and gain in pro-saccade and anti-saccade tasks. This suggests that precise quantitative saccadic testing may be considered as a potential surrogate outcome for cognitive function in longitudinal studies and treatment trials.
**Methods:** Six patients with RRMS and four patients with SPMS were imaged using SD-OCT and a custom built adaptive optics scanning light ophthalmoscope (AOSLO) with confocal and split detection imaging capabilities. Automated retinal segmentation was achieved using the Iowa Reference Algorithms. Inner retinal (IR) thickness, defined as ILM to INL, was assessed using the ‘62 grid’ pattern. The superior and temporal grid regions were extracted to match AOSLO imaging locations. Microvascular images were graded on the presence or absence of capillary bolus formations, saccular/ fusiform formations (SF) and hairpin loops.

**Results:** Two subjects did not have sufficient image quality for microvascular grading so were excluded. In the remaining patients IR thickness in the superior region was similar between the RRMS and SPMS groups; 187 \( \mu \)m (SD: 51.1) and 174 \( \mu \)m (SD: 39.3) respectively. Temporal IR thickness was 156 \( \mu \)m (SD: 45.5) and 152 \( \mu \)m (SD: 24.6) respectively. Microvascular “bolus” formations were most common in the SPMS patient group (90.6% of images) compared with 87.5% from the RRMS group. When present, SF and hairpin loops appeared in conjunction with bolus formations. SF were present at 18.8% in the SPMS and at 16.7% in the RRMS groups and hairpin loops were more common in the SPMS group at 18.8% compared to 12.5% in the RRMS group. There is a significant correlation between IR thickness and bolus formation \((r^2 =0.42; p=0.03)\) but no correlation between the number of formations and retinal thickness or MS disability (EDSS score).

**Conclusions:** Our pilot data suggest that the retinal microvasculature is altered in both relapsing remitting and secondary progressive MS. The similarity in their frequency suggests that this may be an early feature of the disease. Given that capillary abnormalities have previously been seen in brain sections, whether these formations are a cause of MS related disability, or an effect of degeneration, remains an interesting question requiring further study.

**Commercial Relationships:** Sarah Houston, None; Ashwini Nandoskar, None; Richard Nicholas, None; Jeremy Chataway, None; John Greenwood, None; Adam M. Dubis, None

**Support:** The work was supported by grants from the National Institute for Health Research Biomedical Research Centre at Moorfields Eye Hospital National Health Service Foundation Trust, UCL Institute of Ophthalmology and University College London, the Multiple Sclerosis Society, the Rosetrees Trust and Stoneygate Trust. JC acknowledges the UK National Institute for Health Research (NIHR) University College London Hospitals/University College London Biomedical Research Centres Funding scheme. RN acknowledges the UK National Institute for Health Research (NIHR) Imperial College/Imperial College Healthcare Biomedical Research Centres Funding scheme.

**Program Number:** 5119 Poster Board Number: B0006
**Presentation Time:** 8:30 AM–10:15 AM

**Ophthalmological parameters could indicate the safety of nanomembrane plasmapheresis in patients with relapsing-remitting form of Multiple Sclerosis (RRMS) during remission and with Neuromyelitis Optica (NMO) while not experiencing an acute episode of the disease, and the correlation with the lipid peroxidase level - an oxidative stress parameter.**

**Methods:** Two male and three female patients with RRMS and one female patient with NMO were treated with nanomembrane plasmapheresis with serum immunoglobulins and lipid peroxidases levels measurement pre- and post- treatment. Except for one, the patients were treated- free for an average 96 months (at least 8) prior to the plasmapheresis treatment. Previous treatment included interferons for all patients and Fingolimod for two of the patients. The average plasmapheresis procedures per patient was 8.8 (5-11) for an average period of 8 (1-17) months. We evaluated several ophthalmological parameters including: best corrected visual acuity (BCVA), ophthalmological status with biomicroscopy and funduscopy, visual field and peripapillary retinal nerve fiber layer (RNFL) thickness. The follow up period was 24 months for the patient with NMO and an average 13.6 months for the patients with RRMS.

**Results:** All of the patients improved according to the Expanded Disability Status Scale (EDSS) after the treatment and were free of relapses during the follow up period. Reduction of both immunoglobulins and lipid peroxides levels was observed after the plasmapheresis in all patients. Neither progression, nor worsening of the BCVA and the visual field testing results were detected. The RNFL thickness showed thinning in the patient with NMO and thickening in one of the patients with MS. The thinning of the RNFL in the NMO patient, however, could be due to her comorbidity of primary open-angle glaucoma. The mean RNFL thickness in the rest of the patients remained stable.

**Conclusions:** The nanomembrane plasmapheresis is demonstrated as a safe treatment option for the patients with RRMS and NMO not only for the steroid- resistant acute episodes, but also as a basic one during remissions of the RRMS and non-acute episode of NMO as was demonstrated by the stability of the studied ophthalmological parameters.

**Commercial Relationships:** Peter K. Sapundzhiev, None; Petja I. Vassileva, None; Alexander Alexandrov, None; Albena Momchilova, None; Zlatan Tsonchev, None; Milka Orozova, None

**Program Number:** 5120 Poster Board Number: B0007
**Presentation Time:** 8:30 AM–10:15 AM

**The sensitivity of OCT in detecting optic neuritis**
Sarah C. Xu, Jacqueline Leavitt, David Hodge, John J. Chen
1Department of Ophthalmology, Mayo Clinic Hospital, Rochester, MN; 2Department of Biostatistics, Mayo Clinic Hospital, Rochester, MN; 3Department of Neurology, Mayo Clinic Hospital, Rochester, MN.

**Purpose:** Correctly identifying prior optic neuritis is critically important because the presence or absence of optic neuritis may confirm or refute a diagnosis of neurologic conditions, such as multiple sclerosis and neuromyelitis optica. Prior studies have suggested that optical coherence tomography (OCT) has a sensitivity of 68% for detecting prior optic neuritis. However, they used two standard deviations below age matched controls as “abnormal”. This can be an insensitive measure because patients have different baseline thicknesses. We believe that looking at inter-eye differences in cases of unilateral optic neuritis would be more sensitive in detecting prior optic neuritis. Thus, we evaluated the sensitivity of Cirrus OCT in detecting prior unilateral optic neuritis.

**Methods:** We performed a retrospective, observational clinical study of all patients with unilateral optic neuritis who presented (RRMS) during remission and in a patient with Neuromyelitis Optica (NMO) while not experiencing an acute episode of the disease, and the correlation with the lipid peroxidase level - an oxidative stress parameter.
between 2014 and 2016. Patients were included if they had unilateral optic neuritis and had OCT done at least 3 months after the optic neuritis (range of 3–44 months). Optic neuritis was confirmed radiographically in 70.5% of patients and the remainder were diagnosed clinically. We compared OCT retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thicknesses between the affected and unaffected, contralateral eyes. We excluded patients with concomitant glaucoma or other optic neuropathies. Paired T-test was used to compare RNFL and GCL thicknesses between eyes. In calculating sensitivity, thinning was considered significant if the RNFL or GCL was at least 6 μm less in the affected eye compared to the unaffected.

**Results:** A total of forty-four patients (15 male and 29 female) were included in the study. RNFL and GCL thicknesses were significantly lower in eyes with optic neuritis compared to unaffected eyes (p<0.002). RNFL was thinner by ≥6 μm in 84.1% of optic neuritis eyes compared to the unaffected eye. GCL was thinner by ≥6 μm in 95.2% optic neuritis eyes. The sensitivity of OCT in detecting prior optic neuritis was 97.7% when using both average RNFL and GCL thicknesses. When using a cutoff of ≥2 standard deviations below age-matched controls, sensitivities were 59.1% for RNFL, 81.0% for GCL, and 81.8% for either GCL or RNFL thicknesses.

**Conclusions:** OCT is a highly sensitive modality in detecting prior optic neuritis, which is made more robust by using inter-eye differences to approximate change and combining GCL and RNFL data.

**Commercial Relationships:** Sarah C. Xu, None; Jacqueline Leavitt, None; David Hodge, None; John J. Chen, None

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**Purpose:** To evaluate the clinical profile of urgent vision loss due to optic neuritis at a level one trauma center and county hospital in downtown Los Angeles.

**Methods:** An IRB approved, retrospective chart review of 197 patients who received urgent ophthalmological consultation at the Los Angeles County Hospital, University of Southern California Medical Center was performed. 34 patients were identified based on the following targeted search terms: “optic neuritis,” “optic nerve enhancement” on neuroimaging, or constellation of “pain with extraocular movements” and signs of optic nerve disease including decreased color sensitivity and optical coherence tomography findings.

**Results:** Of the 34 patients, 22 were female (64.7%). Twenty-five individuals were Hispanic (73.5%). Prior diagnoses included AIDS (n=1), cocaine use (n=1), diabetes (n=3), hypertension (n=3), anterior uveitis (n=1), and seizures (n=1). Nine of the patients presented with a known diagnosis, i.e. multiple sclerosis (n=3), neuromyelitis optica (n=1), meningioma (n=2), lymphoma (n=1), pituitary mass (n=1), and pseudotumors (n=1).

While the predominant diagnosis was typical optic neuritis, MS, or NMO in 41.2%, other diagnoses included atypical optic neuritis, infectious, compressive, and infiltrative optic neuropathies, neuroretinitis, vasculitic infarct, vasculitic AION, and Vogt-Koyanagi-Harada syndrome.

Of the 14 typical optic neuritis, MS, and NMO patients, two were diagnosed with NMO. Of the 12 remaining patients, the average age was 33 years; 75% were female, 58% presented with pain with extracocular movement, 33.3% had optic disc edema, and 100% had white matter disease, all of which were similar to that of the Optic Nerve Treatment Trial (ONTT) results. Follow-up ranged from one day to ten months, with 64.7% and 29.4% having a final visual acuity <20/40 or <20/200, respectively.

**Conclusions:** The clinical presentation of patients with optic neuritis can overlap with a host of other diagnoses. Sub-group analysis of predominantly Hispanic and Black patients with demyelinating disease revealed similar characteristics to that of the ONTT but potentially suggest poorer visual outcomes than compared to Caucasians. The study is limited by short periods of patient follow-up due to recent diagnosis, suggesting the need for long-term studies regarding the visual outcomes and prognosis of optic neuritis in Hispanics and other minorities.

**Commercial Relationships:** Luv Patel, None; Lilangi S. Edirwicrema, None; Sachi Patel, None; Vivek Patel, None

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**Purpose:** A good recovery from optic neuritis (ON) is usually defined as painless vision loss due to optic neuritis at a level one trauma center and county hospital in downtown Los Angeles.

**Methods:** To improve patient management.

**Methods:** We set out to evaluate visual function after acute ON in a prospective cohort study, and to identify predictors of visual disability that may be readily detected and useful in clinical practice or in clinical trials improves patient management.

**Methods:** We carried out a prospective study on 38 consecutive patients with acute ON followed monthly for 6 months in order to evaluate high and low contrast visual acuity (HCVA) charts, leading to the misconception that ON is a benign condition. However, when more sensitive measurements are used, such as high contrast visual acuity (LCVA), color vision, motion perception or detailed quality of vision scales, patients who have suffered ON often display significant impairments that limit their daily life.

We set out to evaluate visual function after acute ON in a prospective cohort study, and to identify predictors of visual disability that may be readily detected and useful in clinical practice or in clinical trials to improve patient management.

**Results:** Of the 34 patients, 22 were female (64.7%). Twenty-five individuals were Hispanic (73.5%). Prior diagnoses included AIDS (n=1), cocaine use (n=1), diabetes (n=3), hypertension (n=3), anterior uveitis (n=1), and seizures (n=1). Nine of the patients presented with a known diagnosis, i.e. multiple sclerosis (n=3), neuromyelitis optica (n=1), meningioma (n=2), lymphoma (n=1), pituitary mass (n=1), and pseudotumors (n=1).

While the predominant diagnosis was typical optic neuritis, MS, or NMO in 41.2%, other diagnoses included atypical optic neuritis, infectious, compressive, and infiltrative optic neuropathies, neuroretinitis, vasculitic infarct, vasculitic AION, and Vogt-Koyanagi-Harada syndrome.

Of the 14 typical optic neuritis, MS, and NMO patients, two were diagnosed with NMO. Of the 12 remaining patients, the average age was 33 years; 75% were female, 58% presented with pain with extracocular movement, 33.3% had optic disc edema, and 100% had white matter disease, all of which were similar to that of the Optic Nerve Treatment Trial (ONTT) results. Follow-up ranged from one day to ten months, with 64.7% and 29.4% having a final visual acuity <20/40 or <20/200, respectively.

**Conclusions:** The clinical presentation of patients with optic neuritis can overlap with a host of other diagnoses. Sub-group analysis of predominantly Hispanic and Black patients with demyelinating disease revealed similar characteristics to that of the ONTT but potentially suggest poorer visual outcomes than compared to Caucasians. The study is limited by short periods of patient follow-up due to recent diagnosis, suggesting the need for long-term studies regarding the visual outcomes and prognosis of optic neuritis in Hispanics and other minorities.

**Commercial Relationships:** Luv Patel, None; Lilangi S. Edirwicrema, None; Sachi Patel, None; Vivek Patel, None

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**Program Number:** 5122 **Poster Board Number:** B0009

**Presentation Time:** 8:30 AM–10:15 AM

**Early retinal atrophy predicts long-term visual impairment after acute optic neuritis**

**Bernardo Sanchez-Dalmau**, Elena H. Martinez-Lapiscina, Ruben Torres Torres, Santiago Ortiz-Perez, Salut Alba-Arbalat, ANA Guerrero-Zamora, David Calbet, Laura Sanchez-Vela, Pablo Villoslada. *Ophthalmology, Hospital Clinic, Sabadell, Spain; IDIBAPS, Barcelona, Spain; Investigaciones Estadisticas, Barcelona, Spain.

**Purpose:** A good recovery from optic neuritis (ON) is usually defined as painless vision loss due to optic neuritis at a level one trauma center and county hospital in downtown Los Angeles.

**Methods:** We set out to evaluate visual function after acute ON in a prospective cohort study, and to identify predictors of visual disability that may be readily detected and useful in clinical practice or in clinical trials to improve patient management.

**Methods:** We carried out a prospective study on 38 consecutive patients with acute ON followed monthly for 6 months in order to evaluate high and low contrast visual acuity (LCVA), quality of vision (NEI-VFQ-25), visual fields and retinal thickness by spectral domain optical coherence tomography (SD-OCT).

We compared the differences in visual acuity and retinal thickness during the follow-up period, and we developed linear regression models to predict visual function at the end of the 6 month follow-up.

**Results:** The significantly impaired LCVA and color vision in the eye affected by ON persists with respect to the fellow-eye 6 months after acute ON, in association with a significant impact on vision-related QoL. By contrast, high contrast vision and visual fields were less severely impaired. LCVA and color vision was moderately to strongly correlated with the thicknesses of the ganglion cell plus inner plexiform layer (GCIP, L, 2.5% LCVA r= 0.6 and p= 0.0001; color vision r=0.75 and p<0.0001) and that of the peripapillary retinal nerve fiber layer (pRNFL, LCVA r= 0.43 and p= 0.0098; color vision r=0.62 and p=0.0001) measured by OCT. Linear regression models that included the change from baseline to month 1 after onset of the changes in GCIP and pRNFL thicknesses explained 47% of the change in 2.5% LCVA and 67% of the change of color visual acuity.

**Conclusions:** Optic neuritis frequently impairs vision, as revealed by sensitive measures like LCVA and color vision. Monitoring
retinal atrophy by OCT within the first month after ON onset allows individuals at a high risk of residual visual impairment to be identified.

Commercial Relationships: Bernardo Sanchez Dalmau; Elena H. Martinez-Lapisicina, None; Ruben Torres Torres, None; Santiago Ortiz-Perez, None; Salut Alba-Arbalat, None; ANA Guerrero-Zamora, None; David Calbet, None; Laura Sanchez-Vela, None; Pablo Villoslada, None

**Program Number:** 5123 **Poster Board Number:** B0010

**Presentation Time:** 8:30 AM–10:15 AM

In vivo Retinal Structural and Microvascular Changes that Occur in Early Alzheimer’s Disease Using Optical Coherence Tomography Angiography

**William Robert Kwapong**, Meixiao Shen, Peng Chenlei, Shenghai Huang, Fan Lu. The Eye Hospital of Wenzhou Medical University, Wenzhou, China.

**Purpose:** Alzheimer’s disease (AD) is a prevalent, long-term progressive neurodegenerative disorder; besides neurodegeneration, pathological studies have shown that small vessel changes play a role in the pathophysiology of AD. The retinal structure and microvasculature enables the non-invasive visualization and evaluation of the neurovascular system alteration of the brain. The purpose of this study is to quantitatively evaluate the retinal microvascular network and the intra-retinal layer thickness of early AD patients and cognitively normal controls using Optical Coherence Tomography Angiography (OCT-A).

**Methods:** Twelve patients with mild to moderate AD (mean age, 62.56 ± 0.4 years) and ten age-matched control subjects (mean age, 61.25±2.9 years) were enrolled. Retinal images around the macular were obtained by OCT-A. Quantitative intra-retinal layer thickness and microvascular parameters (fractal dimension \(D_f\)) were measured.

**Results:** Patients with AD showed a significantly lower local \(D_f\) of retinal microvasculature in the nasal section. With the retinal structure, a significant thinning of the RNFL was found in the superior inner, superior outer and inferior outer subfields in patients with AD compared with control subjects. A thicker layer was shown by the AD patients in the GCIP when compared with the control subjects. AD patients showed a thicker INL with significant thickening in the central, nasal inner and temporal outer subfields (P<0.05). There was a significant positive correlation between the RNFL and the MMSE (mini mental state examination) \((r=0.59, P=0.05)\). There was a trend of association between the RNFL+GCIP and \(D_f\) of the superficial vascular layer \((r=0.32, P=0.058)\).

**Conclusions:** Patients with early AD had a loss of retinal microvascular network, which may play a role in the initiation of the neurodegenerative process. OCT-A can provide useful information regarding retinal changes in the eyes of patients with AD and help to better understand the mechanisms that contribute to the ongoing processes of AD pathology.

**Commercial Relationships:** William Robert Kwapong; Meixiao Shen, None; Peng Chenlei, None; Shenghai Huang, None; Fan Lu, None

**Program Number:** 5124 **Poster Board Number:** B0011

**Presentation Time:** 8:30 AM–10:15 AM

Quantification of amyloid beta in the eye: Novel biomarkers for Alzheimer’s disease

**Sijia Cao**, Jing Z. Cui, Jiangyuan Gao, Aikun Wang, Sien Lee1,2, Mirza F. Beg, Marinko V. Sarunic, Joanne A. Matsubarad, Ophthalmology, University of Alberta, Edmonton, AB, Canada; 1School of Engineering Science, Simon Fraser University, Burnaby, BC, Canada.

**Purpose:** Alzheimer’s disease (AD) is the most common cause of dementia. It accounts for 60 to 80% of dementias in the elderly and affects approximately 500,000 Canadians. The current clinical tests to confirm AD diagnosis is expensive and can only be used to confirm AD in individuals already having cognitive memory impairment. Developing novel non-invasive and inexpensive techniques that can further identify those who may have incipient but asymptomatic AD is greatly needed. The eye has the same embryonic origin as the brain and they remain tightly interconnected physiologically and functionally. The relationship of amyloid beta (Aβ) load between in the eye and the brain was previously suggested but remains uncertain. In this study, we quantify the Aβ load in the eye and establish proof-of-concept of the relationship between the Aβ load in the eye and concomitant buildup in the brain of transgenic mouse models of AD.

**Methods:** To detect specific species of Aβ, the retina/choroid or brain tissues from transgenic mice (APPswe, PSEN1dE9) were homogenized in ice-cold RIPA buffer containing protease inhibitor cocktail or in 2% SDS alone. Blotting procedures followed our previously established western blot (WB) protocol. The reducing condition is prepared by mixing tissue lysates with 2× reducing loading buffer containing 2% β-mercaptoethanol and boiling for 5 minutes. The two primary antibodies, 6E10 and MOAB2 were used for the detection of Aβ in WB. GAPDH was used as a loading control.

**Results:** Both MOAB2 and 6E10 antibodies revealed several bands in WB results. As expected, MOAB2 did not reveal a band at around 100kDa, the predicted molecular weight (MW) of amyloid precursor protein (APP), while 6E10 detected a band at MW≈100kDa. Protein extraction by RIPA and SDS yielded similar results; while band definition was clearer with reducing compared to non-reducing conditions.

**Conclusions:** We optimized the protocol of WB to detect Aβ species in eye tissues. MOAB2 did not detect APP and yielded more specific results than 6E10. Future work will test the hypothesis that Aβ deposition in the eye is concomitant with the Aβ load in the brain of the mouse model of AD. These findings will drive future work on the role of Aβ on retinal homeostasis as well as the development of a new imaging device for non-invasive detection of retinal Aβ in vivo.

**Commercial Relationships:** Sijia Cao, None; Jing Z. Cui, None; Jiangyuan Gao, None; Aikun Wang, None; Sien Lee, None; Mirza F. Beg, None; Marinko V. Sarunic, None; Joanne A. Matsubara, None

**Support:** Brain Canada and Genome BC

**Program Number:** 5125 **Poster Board Number:** B0012

**Presentation Time:** 8:30 AM–10:15 AM

Retinal Biomarkers for Early Alzheimer’s Disease

Aleid van de Kreeke, Esmeer H. Rumhart, Hoang-Ton Nguyen, Elles Konijnenberg, Theodorus L. Ponsioen, Pieter Jelle Visser, Frank Verbraak, Ophthalmology, VU University Medical Center, Amsterdam, Netherlands; 1Neurology, VU University Medical Center, Amsterdam, Netherlands; 2Ophthalmology, Isala, Zwolle, Netherlands.
**Purpose:** As a protrusion from the brain, the retina might reflect neurodegenerative diseases. There is increasing evidence of changing retinal vasculature and retinal nerve fiber layer (RNFL) thickness in AD patients. This study evaluated these ophthalmological parameters for their potential as early and easily assessable biomarkers for AD.

**Methods:** The potential of retinal vasculature and RNFL as biomarkers for early AD was studied in a cohort of cognitively healthy elderly persons, that will be followed over time. Dynamic amyloid PET scans were acquired using [18F]Flutemetamol, to assess amyloid-beta non-displaceable binding potential (Aβ BPND) in the posterior cingulate. MRI scans were acquired to assess hippocampal volume and intracranial volume. Fundus images of 129 individuals were analyzed and retinal vascular parameters (RVPs), including calibers, tortuosity and fractal dimension, were measured using Singapore I Vessel Assessment (SIVA) software. Peripapillary RNFL thickness of 120 individuals was measured using optical coherence tomography. Firstly, it was investigated whether RVPs are related to Aβ BPND. Secondly, it was investigated whether RNFL thickness is associated with hippocampal volume.

**Results:** Retinal venular changes were associated with Aβ BPND, after adjusting for age, gender and cardiovascular risk factors. Higher Aβ BPND was associated with a smaller central retinal vein equivalent (β=0.004, p=0.049), a higher venular branching coefficient (β=0.342, p=0.024), and a higher venular asymmetry factor (β=0.590, p=0.014). Additionally, a thinner RNFL in the superior (β=8.60, p=0.002) and temporal superior (β=5.62, p=0.005) segment was associated with smaller hippocampal volume, after adjusting for age, gender and intracranial volume.

**Conclusions:** Cognitively healthy individuals with retinal venular changes and thinner RNFL show higher cerebral Aβ BPND in the posterior cingulate and decreased hippocampal volume respectively, suggesting these characteristics are potential biomarkers for early AD. Future follow-up studies will reveal their true value.

**Commercial Relationships:** Aleid van de Kreeke, None; Esmee H. Runhart, None; Hoang-Ton Nguyen, None; Elles Konijnenberg, None; Theodorus L. Ponsioen, None; Pieter Jelle Visser, None; Frank Verbraak, None

**Program Number:** 5126 Poster Board Number: B0013
**Presentation Time:** 8:30 AM–10:15 AM

**Drusen in the Peripheral Retina of the Alzheimer’s Eye**

Kresimir Ukalovic, Sijja Cao, Siuen Lee, Qiaoyue Tang, Mirza F. Beg, Marinko V. Sarunic, Robin Hsiung, Ian R. Mackenzie, Veronica Hirsch-Reinshagen, Jing Z. Cui, Joanne A. Matsubara, Brandon J. McIlmoyle, Siuen Lee, Veronica Hirsch-Reinshagen, Ian R. Mackenzie, Robin Hsiung, Sijja Cao, Qiaoyue Tang, Brennan Eadie, Kailun Jiang, Marinko V. Sarunic, Mirza F. Beg, Jing Z. Cui, Joanne A. Matsubara, Medicine, University of British Columbia, Vancouver, BC, Canada; 2Simon Fraser University, Burnaby, BC, Canada; 3Pathology, University of British Columbia, Vancouver, BC, Canada; 4Ophthalmology, University of British Columbia, Vancouver, BC, Canada; 5Neurology, University of British Columbia, Vancouver, BC, Canada.

**Purpose:** Recent work on Alzheimer’s disease (AD) diagnosis has focused on neuroimaging, in particular CT, MRI and PET; however, neuroimaging is expensive, sometimes invasive and not available to all patients. Ocular biomarkers could provide an alternative way to diagnose AD, and may be more accessible than neuroimaging. Based on previous studies suggesting that peripheral drusen may be useful as an AD biomarker, we tested the hypothesis that peripheral hard drusen would be increased in AD patients compared to controls using post-mortem eye tissues.

**Methods:** We assessed the histological evidence for drusen in postmortem eye tissues obtained from donors with a primary or secondary pathological diagnosis of AD. Retina from normal donors were processed and categorized into younger (<55 years old) and older (>55 years old) groups. After fixation and dissection, 6-μm punches of RPE/choroid were taken in macular (centered on fovea), superior, inferior, and temporal retinal regions. In order to identify drusen, Oil Red - a stain that binds to neutral lipids - was used. Hard drusen were measured, counted and grouped into two size categories: small (≤ 63μm) and intermediate (63-125μm). The number of hard drusen was normalized to the surface area of the punch. Statistical analyses were performed using SPSS.

**Results:** There was a significant increase in the total number of macular hard drusen and peripheral hard drusen in older, compared to younger, normal eyes, as expected (p=0.05). However, significance was not reached for small hard drusen in AD eyes compared to older normal eyes. Interestingly, intermediate hard drusen were more commonly found in the temporal region of AD eyes compared to older normal eyes (p<0.05). Among the brain and eye tissues from AD donors, there was a strong relationship between cerebral amyloid angiopathy (CAA) score and number of intermediate hard drusen in the temporal region of the retina (R2=0.6, p<0.05).

**Conclusions:** Results suggest that peripheral drusen may be useful for further biomarker studies assessing the eye of AD patients, as the number of intermediate hard drusen in the temporal peripheral retina is increased compared to controls, and is positively correlated with CAA severity in corresponding AD brain tissue. Thus, non-invasive fundus imaging of temporal intermediate drusen may have biomarker potential for AD detection and/or progression and is worthy of further investigation.

**Commercial Relationships:** Kresimir Ukalovic, None; Sijja Cao, None; Siuen Lee, None; Qiaoyue Tang, None; Mirza F. Beg, None; Marinko V. Sarunic, None; Robin Hsiung, None; Ian R. Mackenzie, None; Veronica Hirsch-Reinshagen, None; Jing Z. Cui, None; Joanne A. Matsubara, None

**Support:** Brain Canada, Genome BC and VGH+UBC Foundation

**Program Number:** 5127 Poster Board Number: B0014
**Presentation Time:** 8:30 AM–10:15 AM

**Retinal amyloid beta load is associated with cerebral amyloid angiopathy**

Brandon J. McIlmoyle, Siuen Lee, Veronica Hirsch-Reinshagen, Ian R. Mackenzie, Robin Hsiung, Sijja Cao, Qiaoyue Tang, Brennan Eadie, Kailun Jiang, Marinko V. Sarunic, Mirza F. Beg, Jing Z. Cui, Joanne A. Matsubara, Medicine, University of British Columbia, Vancouver, BC, Canada; 2Simon Fraser University, Burnaby, BC, Canada; 3Pathology, University of British Columbia, Vancouver, BC, Canada; 4Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, BC, Canada; 5Neurology, University of British Columbia, Vancouver, BC, Canada.

**Purpose:** Alzheimer’s disease (AD) is a neurodegenerative disorder with excessive amyloid beta (Aβ) deposits in the brain. Diagnosis of AD includes positron emission tomography (PET) measure of the brain Aβ; however, PET is expensive and involves radiation exposure. Recent studies have suggested retinal Aβ as a potential biomarker for AD. The purpose of this study is to assess the Aβ load in the retina in AD and normal donors, and test the hypothesis that retinal Aβ load is related to cerebral amyloid angiopathy (CAA).

**Methods:** Post-mortem brain and retinal tissue from donors with AD (N=11) and non-AD dementia (N=5) and post-mortem retinal tissue from normal, control donors (without dementia) (N=10) were processed. Brain samples were evaluated for neuritic and diffuse senile plaques (CERAD score), Aβ protein (Thal phase), neurofibrillary tangles (Braak stage) and CAA. Retinal samples were processed as free floating punches (4 mm) and paraffin embedded cross sections (6 μm) using mouse monoclonal Aβ antibodies (6F/3D) and Cy3 secondary antibodies. Retinal Aβ was measured on Cy3-stained confocal microscopy images by pixel counting.

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**Results:** AD and non-AD dementia donors with no (N = 4) or mild (N=5) CAA were grouped as CAA1, while those with moderate (N = 3) or severe (N = 4) CAA were grouped as CAA2. The group mean retinal Aβ load of normal control, CAA1, and CAA2 were compared using a two-tailed t-test. CAA2 showed significantly greater retinal Aβ load in all regions than normal controls (p < .001) and CAA1 (p = .004). Between CAA1 and normal control group, significant retinal Aβ load difference was observed only in the temporal region (p = .013).

**Conclusions:** Moderate to high brain CAA levels were associated with high Aβ load in the retina. The results of the study suggest further investigation of the connection between retinal Aβ measurement and brain CAA.

**Commercial Relationships:** Brandon J. McIlmoyle, Sieun Lee, None; Veronica Hirsch-Reinshagen, None; Ian R. Mackenzie, None; Robin Hsiung, None; Sijia Cao, None; Qiaoyue Tang, None; Brenan Edie, None; Kailun Jiang, None; Marinko V. Sarunic, None; Mirza F. Beg, None; Jing Z. Cui, None; Joanne A. Matsubara, None

**Support:** Brain Canada, Genome BC, VGH & UBC Foundation

**Program Number:** 5128
**Poster Board Number:** B0015
**Presentation Time:** 8:30 AM–10:15 AM

**Evaluation of Feasibility and Acceptability of the Convergence Insufficiency Symptom Survey for Concussion (CISS-CON)**

**Among Concussed Youth**

Katherine Weise¹, Jennifer B. Christy¹, Mitchell Scheiman¹, Eric Borsting², Heath Hale³, Sarah D. Lee⁴, Sarah Terry⁴, Laura E. Dreer⁴

¹Pediatric Optometry, University of Alabama at Birmingham, Birmingham, Birmingham, AL; ²Physical Therapy, University of Alabama at Birmingham, Birmingham, AL; ³Southern California College of Optometry, Marshall B. Ketchum University, Fullerton, CA; ⁴Pennsylvania College of Optometry, Salus University, Philadelphia, PA; ⁵Ophthalmology, University of Alabama at Birmingham, Birmingham, Birmingham, AL; ⁶Children’s of Alabama, University of Alabama at Birmingham Sports Medicine, Birmingham, AL; ⁷Arts and Sciences, University of Alabama at Birmingham, Birmingham, AL.

**Purpose:** The literature is rich in evidence showing that the vision system is affected in concussion; however, there is no validated instrument that allows for symptom monitoring of visually-related symptoms in concussed children. The Convergence Insufficiency Symptom Survey has been shown to be valid and reliable in children without concussion, and has been used in large-scale clinical trials. We used a survey-based cross-sectional study in a focus-group setting to evaluate the feasibility and acceptability of an adapted version of the Convergence Insufficiency Symptom Survey for use in children with concussion (“CISS-CON”).

**Methods:** After concussion-management professionals verbally administered the 25-item CISS-CON questionnaire to 8 children (average age = 14, SD = 2.30; 62.5% female) with history of concussion individually, each child completed a written survey containing forced-choice and open-ended questions on patient acceptability of the CISS-CON. Once individually completed, each child convened in a single, hour-long, focus group-style session (4 children per session) to verbally develop and clarify their written feedback.

**Results:** On a scale ranging from 1 (none) to 10 (extreme), children did not appear to be symptomatic for headaches (M = 2.63, SD = 1.99) or dizziness (M = 1.13, SD = 1.64). The 3 minutes it took to administer the CISS-CON questionnaire was reported as “just about right” by 87.5% and “too long” in 12.5%. Most participants (75%) indicated that questions were “not too difficult to understand” and answers choices were “easy to understand” (100%). 87.5% reported that the CISS-CON did not address too many symptoms. A majority felt that the questions were comprehensive; minor edits were offered. Based on the focus group follow-up discussion, there was consensus that the CISS-CON was easy to understand, an acceptable length, did not exacerbate any concussion-like symptoms, and preferred in its current verbal professional-administered format (vs. electronic, e.g.).

**Conclusions:** Concussed pediatric patients with convergence insufficiency appear to find the CISS-CON acceptable and feasible. This instrument may be useful in both clinical care and research for professionals managing post-concussion vision symptoms in concussed children, and may have implications in return-to-learn protocols.

**Commercial Relationships:** Katherine Weise, None; Jennifer B. Christy, None; Mitchell Scheiman, None; Eric Borsting, None; Heath Hale, None; Sarah D. Lee, None; Sarah Terry, None; Laura E. Dreer, None

**Program Number:** 5129
**Poster Board Number:** B0016
**Presentation Time:** 8:30 AM–10:15 AM

**The effect of carotid stenosis on brain morphology and behavior, evaluated for 11 to 13 months, in a rat animal model**

Arieh S. Solomon¹, Anat Nitzan², Nir Rudoler², ³, Yael Piontkevitz³, ³, Goldschleger Eye Research Institute, Tel-Aviv University, Tel-Hashomer, Israel; ²Health Science, Ben Gurion University, Beer Sheva, Israel; ³Shraga Segal School of Microbiology, Ben Gurion University, Beer Sheva, Israel; ⁴Eye Department, Surasky Medical Center, Tel aviv University, Tel Aviv, Israel; ⁵Strauss Center for Computational Neuroimaging, Tel Aviv University, Tel Aviv, Israel.

**Purpose:** Medical society considers that, in human, carotid stenosis of 80% and up might be the cause of clinical symptoms such as transient ischemic attack. When carotid stenosis exists, but no symptoms are expressed, the condition is called: Asymptomatic Carotid Stenosis. Our hypothesis is that carotid stenosis of lesser degree such as 30% to 50% may damage gradually the brain along life time course and be a risk factor of brain disease later in life?!

**Methods:** We used SD, albino, adult, male rats. We had 30 rats devided in three groups of 10 rats. The first group was the control, with no carotid stenosis. The second group passed unilateral carotid occlusion and the third group passed bilateral carotid stenosis. The carotid stenosis was created under deep anesthesia according to the ARVO rules for Animal Care. We used a 7/0 silk surgical suture to create the stenosis. In order to create equal occlusion we used injection needle of different size such as 30G,27G aligned along the carotid artery. We evaluated the amount of lumen that remained using Doppler examination of each rat. The morphology of the brain was evaluated using MRI: Two different MRI protocol were used T2 weighed and DTI. MRI scanning was performed using a 7T MRI scanner (Bruker) with a 30 cm bore and a gradient strength of up t0 400 mT/m. The MRI protocols included coronal T2 weighted images (T2W) and Diffusion tensor imaging. DTI analysis was performed with in-house software, implemented on MATLAB, and FA and MD maps were produced. Behavioral tests: Morris water maze (WNz) and Open Field test. The WNz test is used to asses spatial learning memory and is considered a hippocampal task. The test consists in a pool with water: 1.5 m diameter and 0.6 m depth. A platform is located below the water surface invisible for the rat. Open field test evaluate general locomotor activity.

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**Results:** MRI evaluation revealed brain damage in all bilateral carotid stenosis rats and in three unilateral. No damage in control rats. The damage was located in the dorsal part of the brain. Behavior tasks revealed latency in learning and shortened memory in both groups of bilateral and unilateral carotid stenosis groups.

**Conclusions:** Long term mild carotid stenosis created morphologic brain damage and functional impairment. When regarding this results we suspect that retina might be involved, so vision. We started now histology evaluation of the eyes.

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**Program Number:** 5130  **Poster Board Number:** B0017  
**Presentation Time:** 8:30 AM–10:15 AM  
**Baseline mobility measures and patient perceptions in stroke induced hemianopia**

*Claire Howard, Fiona J. Rowe.* Health Sciences Research, University of Liverpool, Liverpool, United Kingdom.

**Purpose:** To determine whether correlations exist between baseline mobility measures and patient perceptions when assessing levels of adaptation to post-stroke hemianopia.

**Methods:** Stroke survivors with homonymous hemianopia were assessed within four weeks of onset. Subjects undertook the validated mobility assessment course (MAC) to measure the extent to which they scan the environment visually and identify hazards when navigating. The MAC consists of 24 visual markers on both sides of the visual world at varying heights, as well as obstacles for hazard perception. Subjects were timed, recording number of visual targets identified as well as obstacle collision and ability to follow directional arrows. Subjects’ perception of their level of adaptation to visual impairment was measured using direct questioning and activity of daily living questionnaires including visual function questionnaire NEI VFQ-25 and the EQ-5D tool.

**Results:** 5 subjects with mean age 70.8 years (SD=13.6) were assessed (2 male;3 female). During the MAC, for subjects with isolated hemianopia (n=4), the majority of targets (mean=83.5%, SD=11.8) were seen on the hemianopic side despite a subjective patient perception that they had not adapted to the loss of vision. Conversely, where inattention was also present (n=1), the subject missed the majority of targets on the affected side (8% of targets seen) despite reporting no symptoms.

**Conclusions:** Early recruitment results suggest that the MAC has potential as a clinical tool for the assessment of adaptation status to visual impairment. The course has not previously been used for this purpose. A person is said to have adapted to their visual defect when there is no evidence of impaired daily living as well as full awareness of the defect. However, the adaptation process has not been previously explored and requires investigation in order to understand its mechanisms. Our continued research will follow hemianopic subjects and we hypothesise that, over time, subjects showing successful adaptation will: 1) complete the timed MAC in a reduced time, 2) report a reduction in symptoms and 3) report a subjective expression of adaptation. We hypothesise that subjects with combined inattention and hemianopia who adapt over time will complete the MAC with increased identification of targets as they adapt.

**Commercial Relationships:** Claire Howard, Fiona J. Rowe, None
**Support:** NIH fellowship CDRF 2015-01-013

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**Program Number:** 5131  **Poster Board Number:** B0018  
**Presentation Time:** 8:30 AM–10:15 AM  
**The Effect of Topical Prostaglandins on Migraine Headaches**

*Laura Hall1, Venkatesh Brahma1, Robert L. Lesser2, Adeniyi Fisayo1, Martin Wand3, Christopher Teng1.* 1Yale Eye Center, Yale University School of Medicine, New Haven, CT; 2Neuro-ophthalmology, The Eye Care Group, New Haven, CT; 3Consulting Ophthalmologists, PC, Farmington, CT.

**Purpose:** Migraine headaches are a major health burden and cause of disability. Many suffer without adequate short-term treatment and/or long-term control. We observed that treatment with topical prostaglandin analogues decreased the frequency, severity and duration of migraines. We surveyed patients about their migraine symptoms before and after treatment to learn about the changes potentially related prostaglandin use.

**Methods:** We conducted retrospective surveys on 12 patients (4 males, overall average age 58.2 years). Participants were migraine sufferers treated with prostaglandin analogues either in their eyes (1 drop in both eyes as indicated for the treatment of elevated intraocular pressure) or on the fingernail bed (1 drop applied nightly to the lunula of four to six nails and allowed to dry). We collected data on their migraine history and symptoms before and after treatment with prostaglandins using expanded Migraine Disability Assessment (MIDAS) questionnaires. The Wilcoxon Signed-Rank Test was used to calculate the change in migraine frequency, severity, duration and modified MIDAS scores with prostaglandin treatment.

**Results:** Two subjects used prostaglandin eye drops in their eyes (average length of treatment 79.5 months) and 9 subjects used them on their nails (average length of treatment 8.2 months). There was a decrease in the number of headache days from the 3-month period before treatment (mean 25.8 headache days) to the 3-month period following treatment (mean 7.7 headache days) (p<0.05). There was also a decrease in headache severity from 5.8 to 3.5 (scale of 0-10) (p<0.05) and headache duration from 3-12 hours to 1-3 hours (p<0.05). The MIDAS score also reduced from 18.4 to 2.8 (p<0.05).

**Conclusions:** Prostaglandin analogues are FDA approved for the treatment of elevated intraocular pressure applied to the eye. When used in patients with migraine headaches, there was improvement in the frequency, duration and severity of migraine headaches. Prostaglandin analogues could prove to be a novel treatment modality for the management of migraine headaches.

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Commercial Relationships: Laura Hall; Venkatesh Brahma, None; Robert L. Lesser, None; Adeniyi Fisayo, None; Martin Wand, Patent: WO 2015 10606; Company: Manistee Partners (P); Christopher Teng, None

Program Number: 5132 Poster Board Number: B0019
Presentation Time: 8:30 AM–10:15 AM

Indications of mitochondrial dysfunction in Wolfram syndrome
Chiara La Morgia1,2, Michele Carbonelli1, Leonardo Caporali1, Francesca Tagliavini1, Giulia Amore1,3, federico sadun4, Caterina Tonon1, Ludovica Gramigna1, Raffaele Lodi1, Piero Barboni1, Rocco Liguori1,2, Valerio Carelli1,2,1 IRCCS Institute of Neurological Sciences of Bologna, Neurology Clinic, Bellaria Hospital, Bologna, Italy; 2Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy; 3Functional MR Unit - S.Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; 4Ospedale San Giovanni Evangelista, Tivoli, Italy.

Purpose: Wolfram type 1 (WFS1) recessive mutations are associated with Wolfram syndrome (WS), defined by early-onset diabetes mellitus and optic atrophy. A longstanding debate concerns the possible mitochondrial dysfunction in WS, apparently resolved by the identification of causative mutations in wolframin, a protein mostly localized on the endoplasmic reticulum. We here explore the possible occurrence of mitochondrial dysfunction in a case-series of WS patients and report clinical, neuroradiological and ophthalmological findings.

Methods: We investigated a cohort of 11 WFS1 adult cases (34.3 ± 13.4 years). Neuroophthalmological examination included visual acuity, color vision, pupil, visual field, optical coherence tomography, and fundus picture. In a subgroup of patients we also evaluated lactic acid after standardized exercise, brain-MRI, muscle and brain MR-spectroscopy (MRS).

Results: Age at onset of visual loss was 10.1 ± 4.1 years. All but one had diabetes mellitus and 7/9 had abnormal lactic acid after exercise. Brain MRI variably demonstrated cortical, brainstem and cerebellar atrophy and white matter changes. Brain 1H-MRS showed lactic acid traces in 2/7. Muscle 31P-MRS was abnormal in 1/6. Visual acuity was 0.19 ± 0.18 with impaired color vision in all cases, and abnormal pupillary response in 7/11. Fundus oculi demonstrated diffuse pallor in 8/11 (more temporal in 3/8) and temporal pallor in 3/11 (Fig 1). Visual fields demonstrated generalized defect in 9/11 and central scotoma in 2/11 (Fig 2). OCT showed diffuse and severe retinal nerve fiber thinning in all cases compared to age-matched controls (p<0.001).

Conclusions: Neuroophthalmological phenotype has been poorly characterized in WS. Severe optic atrophy, more evident in the temporal sector concordant with a postmortem study showing a mitochondrial pattern of axonal loss, abnormal lactic acid after exercise and some degree of altered MRS (brain and muscle) all point to a mitochondrial dysfunction in WS.

Examples of visual defects in WS. (A) Diffuse defect (B) Central scotoma

Commercial Relationships: Chiara La Morgia; Michele Carbonelli, None; Leonardo Caporali, None; Francesca Tagliavini, None; Giulia Amore, None; federico sadun, None; Caterina Tonon, None; Ludovica Gramigna, None; Raffaele Lodi, None; Piero Barboni, None; Rocco Liguori, None; Valerio Carelli, None

Program Number: 5133 Poster Board Number: B0020
Presentation Time: 8:30 AM–10:15 AM

Cognitive measure may identify atrophy in visual brain regions associated with posterior cortical atrophy
Elizabeth Couser1, Corinne Pettrigrew2, Anja Soldan2, Marilyn S. Albert3,1 Gerontology, University of Maryland, Baltimore, Baltimore, MD; 1Neurology, Johns Hopkins, Baltimore, MD.

Examples of fundus pictures in WS. Upper line: temporal pallor; lower line: diffuse pallor of the optic disc.
Purpose: To determine whether a simple ratio of cognitive measures is related to atrophy in posterior brain regions, as measured on magnetic resonance imaging (MRI) scans, and thereby identifies patients with posterior cortical atrophy (PCA). PCA affects a small percentage of individuals with Alzheimer’s disease (AD) pathology and is characterized by significant visual-perceptual impairment. There are no established diagnostic criteria for PCA and misdiagnosis of PCA is common. This study tested whether a simple ratio score of visual-perceptual performance to memory performance was associated with MRI measures of visual association cortices in a subgroup of patients with suspected PCA.

Methods: Analyses included 142 patients with AD dementia (M age = 74.5) from the Alzheimer’s Disease Neuroimaging Initiative. Ratio scores, reflecting constructional praxis performance (a measure of visual spatial ability) relative to memory performance, were calculated for each patient using subscales of the ADAS-Cog. Atrophy was estimated using structural MRI measures (volume, thickness) of cortical regions involved in visual processing.

Results: Using the ADAS-Cog ratio scores, 12 patients were classified as possible PCA subjects (M age = 69.9). Relative to the typical AD group, the ‘PCA’ group had smaller volumes and lower thicknesses in two visual brain regions (p < .05), and approached significance in a composite score of visual brain regions. Several MRI measures were significantly related to higher scores on the ADAS-cog ratio in the ‘PCA’ subgroup but not in the group with ADAS-cog ratios in the ‘typical’ range (p < .05). Additionally, logistic regressions showed that the degree of atrophy in several regions predicted PCA group status (p < .05).

Conclusions: The results suggest that the ADAS-Cog based ratio score of constructional praxis to episodic memory recall is associated with significant atrophy in posterior cortical regions. This measure may be useful for identifying individuals with suspected PCA.

Commercial Relationships: Elizabeth Couser, None; Corinne Pettrigrew, None; Anja Soldan, None; Marilyn S. Albert, None

Support: NIH T32 grant 5T32AG027668-08

Program Number: 5134 Poster Board Number: B0021
Presentation Time: 8:30 AM–10:15 AM
New insights into malaria retinopathy using optical coherence tomography
Jack Gormley1, Zhanhan Tu2, Viral Sheth1, Frank A. Proudlock2, Karl Seydel1, Terrie Taylor1, Gerald Msukwa2, Nicholas V. Beare2, Simon P. Harding1, Irene Gottlob1
1University of Liverpool, Leeds, United Kingdom; 2University of Michigan, Ann Arbor, MI; 3College of Medicine, Blantyre, Malawi.

Purpose: The presence of malarial retinopathy (MR) confirms the diagnosis of cerebral malaria (CM) and correlates to clinical parameters and disease severity. However, it’s pathogenesis is incompletely understood. For the first time we studied retinal changes of MR using hand-held spectral domain Optical Coherence Tomography (HH-OCT) and compared findings to fundus photos, fluorescein angiography (FA) and histology to further explore MR and CM pathogenesis.

Methods: All children presenting with MR positive CM were recruited (N=26). On admission participants were assessed and treated with artemisinin-based combination therapies. They had dilated fundus exam, colour fundus photography (CFP), FA and HH-OCT of the macular and optic nerve. HH-OCT was performed daily during admission and at 1-month where possible.

Results: Large retinal vessels had abnormal hyper-reflective walls and variable lumina (90% hypo-reflective, 75% hyper-reflective). Those with hyper-reflective walls (no hyper-reflective lumen) had a hyper-reflective ring in the inner retina. Hyper-reflective capillaries were found universally corresponding to the superficial and deep capillary plexi. Hyper-reflective areas (HRAs) in the middle retina (96%), diffuse whitening with or without hemorrhages (36%), cystoid macula oedema (10%) and undulation of inner/outer retina junction (87%) were seen. Whitening on colour fundus photos corresponded to HRAs in the middle retina. HRAs were hypo-reflective on near infrared images. Histological comparison suggests large vessels with hypo-reflective lumina correspond to vessels with late stage parasitized erythrocytes sequestrating around the vessel wall but normal blood in the centre. Hyper-reflective lumina resemble vessels fully filled with parasitized erythrocytes. Vessel changes resolved rapidly after treatment. Moderate to severe hyper-reflective capillaries were present in 61% at admission and reduced to 9% 24hr and 0% 48hr. HRA's were seen 1-month post admission (83%).

Conclusions: In MR OCT vessel changes were unique and likely to represent parasitized erythrocytes sequestrating on the endothelial wall of large and small vessels. HRAs in the middle retina had similar appearance to paracentral acute middle maculopathy on OCT which has been described in ischemic retinal diseases. OCT changes in MR have the potential to identify children needing more intense treatment and monitor parasite clearing during treatment.

Commercial Relationships: Jack Gormley, None; Zhanhan Tu, None; Viral Sheth, None; Frank A. Proudlock, None; Karl Seydel, None; Terrie Taylor, None; Gerald Msukwa, None; Nicholas V. Beare, None; Simon P. Harding, None; Irene Gottlob, None

Support: MRC grants (MR/J004189/1 and MRC/N004566/1), Ulverscroft Foundation, Michigan State University, Blantyre Malaria Project, Foundation for the Prevention of Blindness UK. Diabetes Eye Research Fund UK

Program Number: 5135 Poster Board Number: B0022
Presentation Time: 8:30 AM–10:15 AM
Subclinical changes on hand-held optical coherence tomography in apparently malaria retinopathy-negative patients with cerebral malaria
Zhanhan Tu1, Jack Gormley1, Viral Sheth1, Frank A. Proudlock1, Karl Seydel1, Terrie Taylor1, Gerald Msukwa2, Nicholas V. Beare2, Simon P. Harding1, Irene Gottlob1, 1Neuroscience, Psychology and Behaviour, University of Leicester, Leicester, United Kingdom; 2University of Liverpool, Leeds, United Kingdom; 3University of Michigan, Ann Arbor, MI; 4College of Medicine, Blantyre, Malawi.

Purpose: There are approximately 214 million malaria cases annually. Of the African children with cerebral malaria (CM) 15% die and 30% have long-term neurological sequelae. Diagnosis of CM can be difficult. Retinal changes closely reflect cerebral changes, thus helping CM diagnosis. Clinical signs of malarial retinopathy (MR) (retinal whitening; vessel discoloration; hemorrhages; papilledema) not only help detect CM but also predict severity. However, one-third of CM patients are MR-negative by funduscopic examination. Also, on autopsy, 30% of patients dying of coma and positive for malaria parasites end up having alternative diagnosis. Therefore it is important to detect subtle retinal changes in funduscopy negative patients. This study used hand-held optical coherence tomography (HH-OCT) for the first time for this purpose.

Methods: Five funduscopy-negative patients with CM were recruited from the Queen Elizabeth Central Hospital, Blantyre, Malawi. All underwent full medical assessments, dilated funduscopys, photography, fluorescein angiography and HH-OCT scans (7 x 7 x 2mm volume for each A scan, 1000 A scans per B scan, 140 or 210 B scans) for fovea and optic nerve on admission once they had been
stabilised after treatment. OCT findings were compared with those observed in retinopathy positive CM patients (n=26) and local age-matched children were used as controls.

**Results:** HH-OCT showed that all 5 retinopathy negative patients had the changes typically observed in MR. Four had hyper-reflective vessel walls with hypo-reflective lumina, 3 had hyper-reflective vessels with hyper-reflective lumina and one had numerous hyper-reflective capillaries. The hyper-reflective vessels and capillaries are consistent with parasitized erythrocytes segregating on the vessel walls, as described histologically.

**Conclusions:** HH-OCT can detect subclinical retinal changes in patients with CM. OCT may increase the accuracy of CM diagnosis in funduscopically negative patients, enabling specific therapeutic intervention. In the future, studies of HH-OCT in a larger number of retinopathy negative patients and correlation with autopsy findings are necessary.

**Commercial Relationships:** Zhanhan Tu; Jack Gormley, None; Viral Sheth, None; Frank A. Proudlock, None; Karl Seydel, None; Terrie Taylor, None; Gerald Msukwa, None; Nicholas V. Beare, None; Simon P. Harding, None; Irene Gottlob, None; Support: MRC grants (MR/J004189/1 and MRC/N004566/1), Ulverscroft Foundation, Michigan State University, Blantyre Malaria Project, Foundation for the Prevention of Blindness UK.

**Program Number:** 5136 **Poster Board Number:** B0023 **Presentation Time:** 8:30 AM–10:15 AM **Quantifying Visual Photosensitivity in Veterans with Traumatic Brain Injury**

Mariela C. Aguilar, Alex Gonzalez, Cornelis J. Rowaan, Anat Galor, Nilj Gregori, Heather A. Durkee, Potyra R. Rosa, Byron L. Lam, Jean-Marie A. Parel, Shihab S. Asfour. ‘Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL; 2Department of Industrial Engineering, College of Engineering, University of Miami, Coral Gables, FL; 3Bascom Palmer Eye Institute, Department of Ophthalmology, University of Miami Miller School of Medicine, Miami, FL; 4VA Medical Center, Miami, FL; 5Brien Holden Vision Institute and Vision Cooperative Research Centre, Sydney, NSW, Australia.

**Purpose:** Traumatic brain injury (TBI) is a significant health issue which affects service members and veterans during times of both peace and war. The Department of Defense and the Defense and Veteran’s Brain Injury Center estimate that 22% of all combat casualties are brain injuries. The purpose of this study was to determine if visual photosensitivity thresholds (VPT) in veterans with TBI could be quantified using the Ocular Photosensitivity Analyzer (OPA) and compare the results with healthy subjects.

**Methods:** The OPA (Aguilar MC, et al. IOVS, 2016; 57(12):622) produces a light stimuli with varying intensities from 1 to 32,000 lux (0 to 4.51 log lux). The subject is instructed by the OPA to indicate whether the light stimulus is “uncomfortable” by pressing a handheld button. After 10 response reversals, the VPT is automatically calculated. To ensure reliability, catch trials were incorporated throughout the test. We compared the VPT of healthy and TBI subjects presenting with light sensitivity symptoms. Three TBI subjects (3 males, age = 64 ± 19) with occurrence of injuries varying in time (2-6 decades), and nine healthy subjects (5 females and 4 males, age = 31.4 ± 7.6) were tested under an IRB approved protocol.

**Results:** The healthy and TBI subjects were found to have a mean predicted VPT of 3.24±0.63 and 0.35±0.61 log lux, respectively. A one-way analysis of variance showed a statistically significant difference (p=0.0001) between the healthy and TBI subject groups.

**Conclusions:** The OPA is a safe and sensitive instrument capable of determining VPT in both healthy and TBI subjects. The findings demonstrate a significant difference in VPT between the groups.

Ongoing studies are being performed with the OPA to increase our subject population and further validate our findings. Furthermore, as treatments for TBI are being developed the OPA has the potential to be utilized as an outcome measure in studies that would warrant a pre-treatment baseline and post-treatment VPT.


**Commercial Relationships:** Mariela C. Aguilar, None; Alex Gonzalez, None; Cornelis J. Rowaan, None; Anat Galor, None; Nilj Gregori, None; Heather A. Durkee, None; Potyra R. Rosa, None; Byron L. Lam, None; Jean-Marie A. Parel, None; Shihab S. Asfour, None; Support: NEI R24 EY020223, DAMD-W81XWH-09-1-0675, DOD Warfighters Grant W81XWH-13-1-0048, Florida Lions Eye Bank, Drs. KR Olsen & ME Hildebrandt, Drs. Raksha Urs & Aaron Furtado, Brien Holden Vision Institute, NIH Center Grant P30EY14801, Research to Prevent Blindness, Henri and Flore Lesieur Foundation (JMP).

**Program Number:** 5137 **Poster Board Number:** B0024 **Presentation Time:** 8:30 AM–10:15 AM **Spectral Domain Optical Coherence Tomography Identifies Outer Retina Thinning in Frontotemporal Lobar Degeneration**


**Purpose:** Alzheimer’s disease (AD) is associated with thinning of inner retina layers (retinal nerve fiber layer and ganglion cell layer) on spectral domain optical coherence tomography (SD-OCT). Frontotemporal lobar degeneration (FTD) is an age-related dementia with distinct pathology, and up to 30% of clinically diagnosed FTD cases have a neuropathological diagnosis of AD. We determined if the retina has biomarker potential for FTD.

**Methods:** We consecutively enrolled 38 cases with clinical FTD (mean age 66 years) and 44 controls (mean age 56 years). Cases were diagnosed by a neurologist. Subgroups of presumed molecular pathology (tauopathy, TAR DNA Binding Protein-43, AD, and unknown pathology) were determined by clinical diagnosis, a cerebrospinal fluid biomarker (total tau:amyloid β 1-42), and genetic markers to identify presumed FTD subtypes and AD. Retinal structure was examined with a standard SD-OCT (Spectralis, Heidelberg Engineering, Carlsbad, CA) protocol and retinal layers segmented by a masked analyst with the Iowa Reference Algorithm (v3.6) for a standard ETDRS (Early Treatment Diabetic Retinopathy Study) grid. Eyes with poor image quality, glaucoma or optic nerve disease, high refractive error, or macular disease were excluded. SD-OCT parameters were compared between eyes of cases (n=50 eyes) and controls (n=69 eyes) using a generalized linear model that accounted for inter-eye correlation.
Results: Controlling for age, sex, and race, the cases had a thinner outer retina than controls (p < 0.05, Table 1). There was thinning of the outer nuclear layer (ONL) and ellipsoid zone (EZ) in cases (p < 0.05, Table 1), and the ONL was the main driver of outer retina thinning. Cases and controls had similar thicknesses for inner retinal layers (Table 1). Subgroup analysis demonstrated that the presumed FTD tauopathy subgroup (n=31 eyes) had thinner ONL and EZ than controls (p < 0.05), and all other subgroups but the presumed AD subgroup showed a trend of ONL thinning (Table 2).

Conclusions: In contrast to AD, FTD is associated with predominant thinning of the outer retina rather than the inner retina.

Table 1. Comparisons of Retinal Layer Thicknesses Between Frontotemporal Degeneration Cases and Normal Controls

<table>
<thead>
<tr>
<th>Retina Layer(s) (Average of 5 central ETDRS grid regions)</th>
<th>Control (N = 44 subjects, 88 eyes)</th>
<th>FTD Cases (N = 50 subjects, 50 eyes)</th>
<th>P – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Retina</td>
<td>Mean (Standard Error) in microns</td>
<td>Mean (Standard Error) in microns</td>
<td>0.22</td>
</tr>
<tr>
<td>Outer Retina (Outer Nuclear Layer to Interdigitation Zone)</td>
<td>304 (2.4)</td>
<td>299 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Outer Nerve Fiber Layer</td>
<td>142 (1.6)</td>
<td>132 (2.0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Ganglion Cell Layer</td>
<td>23.3 (0.5)</td>
<td>22.5 (0.6)</td>
<td>0.41</td>
</tr>
<tr>
<td>Inner Plexiform Layer</td>
<td>40.7 (1.4)</td>
<td>41.9 (1.5)</td>
<td>0.63</td>
</tr>
<tr>
<td>Inner Nuclear Layer</td>
<td>35.5 (0.6)</td>
<td>35.3 (0.6)</td>
<td>0.78</td>
</tr>
<tr>
<td>Outer Plexiform Layer</td>
<td>25.3 (0.6)</td>
<td>28.3 (1.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>Outer Nuclear Layer</td>
<td>98.0 (1.4)</td>
<td>89.0 (1.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Ellipsoid Zone</td>
<td>15.1 (0.1)</td>
<td>14.4 (0.2)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

*From the generalized estimating equations that account for inter-eye correlation. Adjusted for age, sex, and race.

Table 2. Comparisons of Retinal Layer Thicknesses Between Subgroups of Frontotemporal Degeneration Cases and Normal Controls

<table>
<thead>
<tr>
<th>Subgroup Description</th>
<th>Control (N = 44 subjects, 88 eyes)</th>
<th>FTD Cases (N = 50 subjects, 50 eyes)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>tauopathy</td>
<td>Mean (Standard Error) in microns</td>
<td>Mean (Standard Error) in microns</td>
<td></td>
</tr>
<tr>
<td>Total Retina</td>
<td>303.2 (2.3)</td>
<td>295.2 (2.9)</td>
<td>0.13</td>
</tr>
<tr>
<td>Outer Retina (ONL)</td>
<td>142.1 (1.8)</td>
<td>133.2 (2.7)</td>
<td>0.13</td>
</tr>
<tr>
<td>Outer Nerve Fiber</td>
<td>25.2 (0.6)</td>
<td>27.9 (1.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>Ganglion Cell Layer</td>
<td>40.7 (1.4)</td>
<td>41.9 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Inner Plexiform Layer</td>
<td>35.5 (0.6)</td>
<td>35.3 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Outer Plexiform Layer</td>
<td>25.3 (0.6)</td>
<td>28.3 (1.2)</td>
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<td></td>
</tr>
</tbody>
</table>

*Compared to controls and adjusted for age, sex, and race. From the generalized estimating equation that accounts for inter-eye correlation.

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