Optic neuritis / Optic nerve

Thursday, May 07, 2015 8:30 AM–10:15 AM
Exhibit Hall Poster Session

Program #/Board #/Range: 5528–5560/B0099–B0131
Organizing Section: Eye Movements / Strabismus / Amblyopia / Neuro-Ophthalmology
Contributing Section(s): Biochemistry/Molecular Biology, Clinical/ Epidemiologic Research, Visual Neuroscience

Program Number: 5528 Poster Board Number: B0099
Presentation Time: 8:30 AM–10:15 AM
Neuroprotective Effects of Amniotic-derived Cellular Cytokine Solution (ACCS) in Experimental Optic Neuritis


Purpose: Optic neuritis is a demyelinating inflammation of the optic nerve that often occurs in multiple sclerosis (MS) patients. Loss of retinal ganglion cells (RGCs) and their axons also occurs in optic neuritis, and correlates with permanent vision loss. ACCS is a novel biologic mixture of growth factors and cytokines secreted from Amni-on-derived Multipotent Progenitor (AMP) cells, that exhibits anti-inflammatory and neuroprotective properties in a variety of disease models. The ability of ACCS to suppress optic neuritis in the experimental autoimmune encephalomyelitis (EAE) model of MS was examined.

Methods: EAE was induced in C57/BL6 mice by immunization with myelin oligodendroglial glycoprotein peptide. Mice were treated daily with one drop (6 uL) of ACCS intranasally beginning before or after onset of optic neuritis. Visual function was assessed by optokinetic responses (OKR) at baseline, then weekly until sacrifice 6 weeks post-immunization. Retinas and optic nerves were isolated. RGCs were immunolabeled with Brn3a antibodies to quantify RGC survival. Inflammation was assessed by H&E and Iba-1 (macrophage/ microglia marker) staining, demyelination by luxol fast blue staining, and axon and axonal loss by neurofilament staining of optic nerve sections.

Results: Progressive decreases in OKR occurred in vehicle-treated EAE mice, along with significant RGC loss, consistent with prior studies showing onset of optic neuritis occurring 12-15 days after EAE induction. Daily intranasal ACCS treatment beginning on day 0 (day of immunization), 15, 22, or 30, significantly reduced the level of vision loss, and treatment from day 0 or day 15 significantly attenuated RGC loss. ACCS also decreased the degree of demyelination and axonal loss, but had limited effects on the level of inflammation in the optic nerve.

Conclusions: ACCS treatment attenuates RGC loss, preserves OKR responses, and reduces demyelination and axonal loss during experimental optic neuritis in EAE mice. ACCS exerts effects with treatment initiated before and after onset of optic neuritis, suggesting it may be useful as a preventative or abortive therapy. Results suggest ACCS is a potential treatment for optic neuritis that warrants further study. Furthermore, potent effects seen after intranasal administration suggest this may be a novel drug delivery method for optic neuritis.

Commercial Relationships: Reas Sulaimankutty, None; Kimberly Dine, None; Helayna Brown, None; Larry R. Brown, Stemnion Inc (I); Kenneth S. Shindler, Stemnion Inc (F)
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Program Number: 5529 Poster Board Number: B0100
Presentation Time: 8:30 AM–10:15 AM
Experimental optic neuritis induced by the microinjection of lipopolysaccharide into the optic nerve

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Purpose: Optic neuritis (ON) is a condition involving primary inflammation, demyelination, and axonal injury in the optic nerve which leads to retinal ganglion cell (RGC) loss, and visual dysfunction. We investigated the ability of a single microinjection of bacterial lipopolysaccharide (LPS) directly into the optic nerve to induce functional and structural alterations compatible with ON. For this purpose, optic nerves from male Wistar rats remained intact or were injected with vehicle or LPS.

Methods: The effect of LPS was evaluated at several time points post-injection in terms of: i) visual pathway and retinal function (visual evoked potentials (VEPs) and electroretinograms, (ERGs), respectively), ii) anterograde transport from the retina to its projection areas, iii) consensual pupil light reflex (PLR), iv) optic nerve histology, v) microglia/macrophage reactivity (by Iba-1 and ED1-immunostaining), vi) astrocyte reactivity (by glial fibrillary acid protein-immunostaining), vii) axon number (by toluidine blue staining), viii) demyelination (by myelin basic protein immunoreactivity and luxol fast blue staining), viii) optic nerve ultrastructure, and ix) RGC number (by Brn3a immunoreactivity).

Results: LPS induced a significant and persistent decrease in VEP amplitude and PLR, without changes in the ERG. In addition, LPS induced a deficit in anterograde transport, and an early inflammatory response consisting in an increased cellularity, and Iba-1 and ED1-immunoreactivity in the optic nerve, which were followed by changes in axonal density, astrocytosis, demyelination, and axon and RGC loss.

Conclusions: These results suggest that the microinjection of LPS into the optic nerve may serve as a new experimental model of primary ON.

Commercial Relationships: Marcos Luis Aranda, None; Damian Dorfman, None; Pablo Sande, None; Ruth E. Rosenstein, None
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Program Number: 5530 Poster Board Number: B0101
Presentation Time: 8:30 AM–10:15 AM
Impaired axonal transport in a rodent model of optic neuritis due to NMO spectrum disorder

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Purpose: We previously reported that exposure of serum from patients with seropositive neuromyelitis optica spectrum disorders (NMOSDs) led to astrocytic damage at 7 days. However, axonal loss was not detected at that time (Matsumoto Y, et al. Exp. Eye Res. 2014). The purpose of this study was to evaluate whether axonal transport is impaired in a rodent model of optic neuritis in NMOSDs.

Methods: We collected serum from patients with idiopathic or NMO-optic neuritis or from normal subjects. Using male Sprague-Dawley rats (200-300g), we exposed the rat optic nerve to the collected serum as previously reported. The treated rats were divided into those exposed to aquaporin 4 (AQP4) autoantibody-positive serum (AQP4+) or those exposed to AQP4 antibody-negative serum (AQP4−). Seven days (7D) and 14 days (1D) after treatment, rats

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were sacrificed and the optic nerves were excised. Cryosections of the optic nerves were subjected to immunohistochemistry against neurofilament (NF) and kinesin-1-kif5b (Kif5b). Real-time polymerase chain reaction (RT-PCR) analyses were also conducted to evaluate Kif5b gene expressions.

**Results:** Linear Kif5b immunoreactivity (IR) was co-localized with NF expression in the optic nerves. Aggregated IR of Kif5b was scattered in the optic nerves of the AQP4+ group at 7D. The number of the aggregated Kif5b IR in the AQP4+ group was statistically increased than that in the AQP4- group (n=8 each, unpaired t-test; p=0.02). The gene expression of Kif5b was significantly decreased in the AQP4+ group at 14D compared with controls (n=6 each, unpaired t-test; p=0.02), but not in the AQP4- group.

**Conclusions:** Given that kinesin-1-Kif5b plays a critical role in the anterograde axonal transport, the present study suggested that axonal transport is impaired in the optic nerves of rodent models of NMOSDs before detectable axonal loss.

**Commercial Relationships:** Yoshiko Kanamori, None; Akiyasu Kanamori, None; Sho Nobuyoshi, None; Ichiro Nakashima, None; Makoto Nakamura, None

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**Program Number:** 5531 **Poster Board Number:** B0102 **Presentation Time:** 8:30 AM–10:15 AM

Phosphatase and Tensin Homolog (PTEN) Knockout in Retinal Ganglion Cells (RGCs) Rescues Optic Neuritis in Experimental Autoimmune Encephalomyelitis (EAE) Mice

**Venu Talla,** Vince Chiodo, Vittorio Porciatti, Sanford L. Boye, William W. Hauswirth, John Guy.

**Purpose:** To rescue vision loss and optic neuropathy in EAE mouse model using ssAAV2Cre-GFP mediated knockout (KO) of floxed PTEN (PTEN fl/fl), a negative regulator of mTOR (mammalian target of rapamycin) pathway involved in optic nerve axonal regeneration in RGCs.

**Methods:** EAE was induced in floxed-PTEN mice (n=11) and littermates (n=8) by subdermal injection of 0.1 ml homologous spinal cord emulsion in complete Freunds adjuvant in the nuchal area. EAE sensitized floxed-PTEN mice received an intravitreal injection of ssAAV-Cre-GFP into both eyes whereas EAE littermates received ssAAV-mCherry as an injection control. Unsensitized littermates with or without ssAAV-mCherry injections acted as additional controls (n=16). Visual function was assessed by recording pattern electroretinograms (PERG). Spectral domain OCT evaluated the thickness of the inner plexiform layer to the nerve fiber layer at 1, 4 and 9 months post injection (MPI). Expression of the Cre-GFP in the RGCs and ONs were evaluated in live mice by confocal scanning laser ophthalmoscopy (CSLO) imaging at 5 and 9 MPI. Retina and ON tissues were dissected and Tuj1 labeled RGCs and ON axons were evaluated by immunofluorescence.

**Results:** Expression: CSLO imaging at 5 and 9MPI in live EAE floxed-PTEN mice revealed expression of Cre-GFP in RGC layer. Rescue: PERG analysis at 1M, 4M and 9MPI showed a 25%, 37% and 41% reduction in amplitude of EAE-mCherry mice compared to mCherry/control mice (p<0.005). The PERG latencies were also delayed by 7%, 17% and 27% in EAE-mCherry at 1M, 4M (p<0.05) and 9MPI (p<0.05). Interestingly, knockout of PTEN in EAE mice RGCs by AAV2-Cre-GFP injection rescued the amplitudes by 51, 54 and 77% (p<0.005) at 1, 4 & 9MPI. However, the latencies were not significantly rescued compared to EAE-mcherry. OCT images of the EAE-mCherry mice showed a significant thinning (p<0.005) in RNFL/RGC/inner plexiform layers while the OCT images of the PTEN (KO) EAE mice were 150% (p<0.0001) & 122% (p<0.0001) thicker compared to control at 5 & 9 MPI. Quantitative analysis of Tuj1 positive cells revealed 57% rescue of RGCs in PTEN (KO) mice compared to EAE mice (p<0.05).

**Conclusions:** PTEN is involved in intrinsic axonal growth arrest and knocking out the PTEN in RGCs is a strategy that may be useful for treating the 8% of optic neuritis patients experiencing permanent loss of vision.

**Commercial Relationships:** Venu Talla, None; Vince Chiodo, None; Vittorio Porciatti, None; Sanford L. Boye, None; William W. Hauswirth, AGT (F); John Guy, None

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**Program Number:** 5532 **Poster Board Number:** B0103 **Presentation Time:** 8:30 AM–10:15 AM

Changes of CXCL12, CXCL14 and PDGF levels in the brain of patients with idiopathic demyelinating optic neuritis and neuromyelitis optica

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**Purpose:** The CXC chemokines (CXC-motif ligand 12 and CXC-motif ligand 14) and platelet-derived growth factor are suggested to modulate remyelination in the course of many demyelinating diseases. The present study compared the difference in the brain levels of these chemokines between patients with idiopathic demyelinating optic neuritis (IDON) and neuromyelitis optica (NMO) by measuring concentrations of these chemokines in the cerebrospinal fluid using an enzyme linked immunosorbent assay.

**Methods:** In this study, PDGF, CXCL12 and CXCL14 levels in the CSF of IDON and NMO patients were measured by ELISA and compared, and non-inflammatory neural disease (NIND) patients were used as negative control as reported by others.

**Results:** Our data indicate that the prognosis of neuritis depends on the remyelinating process that is impaired due to decreased chemokines. The much lower levels of chemokines would specifically indicate the severe neuritis, such as NMO.

**Conclusions:** In conclusion, the present study strongly suggests that chemokines, PDGF, CXCL12 and CXCL14, may alone and/or together associate with these two types of ON. The former two would serve to stimulate the maturation of OPCs, and the last one is a possible OPC maturation inhibitor.

**Commercial Relationships:** Tingjun Chen, None

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**Program Number:** 5533 **Poster Board Number:** B0104 **Presentation Time:** 8:30 AM–10:15 AM

Color code contrast testing adds predictive value of visual function in combination with low-contrast testing in multiple sclerosis

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**Purpose:** Low contrast visual function has been validated as an important clinical outcome measure in both observational and therapeutic investigational studies in multiple sclerosis. Computerized tests of visual performance provide convenient measures of visual function in the clinic. Subjects with multiple sclerosis frequently have structural injury to the retina that can
be assessed via spectral-domain optical coherence tomography. Recent advances in software algorithms allow segmentation and quantification of individual retinal layers.

Methods: We performed Rabin cone contrast testing (CCT), computerized low contrast threshold testing (LCT), and Heidelberg Spectralis spectral-domain optical coherence tomography (SD-OCT) in 52 people with multiple sclerosis (MS) (102 eyes, 71% female, 18 with a history of a prior optic neuritis). Linear mixed-models were used to analyze the association between cone-contrast and low-contrast visual function and retinal layer thickness, adjusting for age, sex, history of optic neuritis, and accounting for intra-subject inter-eye correlations.

Results: Red, Blue, and Green CCT scores were positively correlated with macular ganglion cell / inner plexiform layer (GCIPL) thickness (p<0.001), were not significantly associated with the thickness of other retinal layers. Linear mixed-effect regression models predicting GCIPL thickness showed significant improvement with the addition of LCT scores (change in deviance of 79.0 and 81.0 in models with and without CCT, respectively). The addition of CCT had a lower magnitude but significant effect on model deviance even when low contrast vision was included as a predictor in the model (change in deviance of 33.6 and 27.4 on models with and without LCT, respectively).

Conclusions: Color cone contrast testing is correlated with GCL thickness in MS and provides added predictive value of visual pathway injury in combination with low-contrast testing in MS patients.

Commercial Relationships: Hao Yiu, None; Samuel Arnow, None; Jeffrey Gelfand, Journal Watch Neurology (Massachusetts Medical Society) (R), Medical Legal Consulting (C); Christopher Songster, None; Denise Bolivar, None; Ari Green, Accorda (C), Biogen (C), Biogen/Idec/Applied Clinical Intelligence (R), Novartis (C), Prana Bioscience (C), Roche (C)

Program Number: 5534 Poster Board Number: B0105
Presentation Time: 8:30 AM–10:15 AM

Visual outcome predictors in acute optic neuritis
Sangah Kim, Samin Hong, Chan Yun Kim, Gong Je Seong.
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Purpose: To find the visual outcome predictors in patients who received intravenous steroid pulse therapy (ISPT) due to acute optic neuritis (AON).

Methods: A retrospective, observational, clinical study. A total of 33 AON patients received ISPT (methylprednisolone, 250 mg, four times a day, 3 days) and had follow-up checkups for at least 3 months after the therapy were included in this study. Patients were divided into two groups, those who finally recovered their vision over LogMAR 0.3 (Group 1, n=25) vs. those who didn’t (Group 2, n=8). We evaluated the demographics and clinical characteristics and tried to determine which factors had affected the visual outcome.

Results: The presence of a relative afferent pupillary defect (RAPD) and a pattern of visual field (VF) defect at presentation, and the degree of visual loss at the 3 month and 1 year after treatment were associated to the final visual outcome. While, age, gender, bilaterality, moving pain, headaches, and the degree of vision and color sense loss were not related to the final visual outcome. The presence of disc swelling and retinal nerve fiber layer (RNFL) defect, the abnormal responses on visual evoked potential (VEP), the abnormal level of erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) were also not associated with the final visual outcome.

Conclusions: At presentation, the RAPD and VF defect excluding visual loss were associated with the final visual outcome in AON patients who had received ISPT. Regarding vision, the visual acuity at 3 months and 1 year after treatment were associated with the final visual outcome.

Commercial Relationships: Sangah Kim, None; Samin Hong, None; Chan Yun Kim, None; Gong Je Seong, None

Program Number: 5535 Poster Board Number: B0106
Presentation Time: 8:30 AM–10:15 AM

Retinal Sensitivity Reduced in Patients with Neuromyelitis Optica Spectrum Disorder with no History of Optic Neuritis
Ryutaro Akiba1, Hirotaka Yokouchi1, Takayuki Baba1, Toshiyuki Oshitari1, Setsu Sawai1, Masahiro Mori1, Satoshi Kuwabara2, Shuichi Yamamoto1, 1Ophthalmology and Visual Science, Chiba University Graduate School of Medicine, Chiba, Japan; 2Department of Neurology, Chiba University Graduate School of Medicine, Chiba, Japan.

Purpose: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory autoimmune disease that can cause severe optic neuritis (ON) and myelitis. The results of previous studies have suggested that early structural changes of retina were present in patients with multiple sclerosis (MS) who have no history of ON. However, there has been very few reports of functional or structural changes in patients with NMOSD who have no history of ON. The purpose of this study was to determine the retinal sensitivity by microperimetry and retinal structure by spectral-domain optical coherence tomography (SD-OCT) in patients with NMOSD who have no history of ON. In addition, we compared the early functional and structural changes of the retina of patients with NMOSD to that of healthy controls.

Methods: Twelve eyes of 6 patients with NMOSD who had no history of ON were studied, the NMOSD group. We determined the retinal sensitivity of the central 100 (37 points) and central 20 (13 points) by macular integrity assessment (MAIA). We also measured the best-corrected visual acuity (BCVA) expressed in logarithm of minimum angle of resolution (logMAR) units and retinal structure by SD-OCT. We quantified the mean thickness of the retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) from the OCT images. Twenty-five eyes of 13 volunteers who had no high myopia, glaucoma, or other macular disorders were included in the HC groups.

Results: There was no significant difference in the BCVA (P=0.168), age (P=0.321), and refractive error (P=0.549) between the NMOSD and HC groups. The retinal sensitivity of the central 100 (NMOSD, 27.65±1.75 dB; HC, 29.12±0.85 dB) and 2 degrees (NMOSD, 27.68±1.96 dB; HC,29.41±1.12 dB) were significantly lower in the NMOSD group (P=0.015 and P=0.015 respectively, Mann-Whitney U-test). The RNFL thickness (NMOSD, 109.5±14.6 μm; HC, 107.2±7.4 μm), and GCL thickness(NMOSD, 94.7±12.0 μm; HC, 97.5±5.2 μm) were not significantly different between the two groups (P=0.527, P=0.557 respectively, Mann-Whitney U-test).

Conclusions: These results indicate that the retinal sensitivity is impaired even before the development of ON in NMOSD patients, and also that the functional impairments precede the structural impairments. Although further investigations are needed, microperimetry appears useful to determine subclinical change of retina in eyes with NMOSD.

Commercial Relationships: Ryutaro Akiba, None; Hirotaka Yokouchi, None; Takayuki Baba, None; Toshiyuki Oshitari, None; Setsu Sawai, None; Masahiro Mori, None; Satoshi Kuwabara, None; Shuichi Yamamoto, None

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Evaluation of ganglion cell complex after optic neuritis by OCT
Annalisa Costa1, Christian Cordano2, Antonella Panizzii3, Laura Landi3, Federico Bisio3, Alessandro Bagnis4, Carla E. Traverso5, antonio ucelli3, Antonio Ferreras3, Michele M. Iester1. 1DINOGMI, University of Genoa Eye Clinic, Genova, Italy; 2DINOGMI, University of Genoa, Clinica Neurologica, Genova, Italy; 3University eye clinic, Zaragoza, Spain.

Purpose: To compare the macular assessment and RNFL thickness by using two different OCTs: a time domain (TD) and a spectral domain (SD) OCT, in patients with unilateral optic neuritis.

Methods: This is a retrospective study. 34 multiple sclerosis (MS) subjects with a single unilateral optic neuritis (ON) were included in the study. An ophthalmological examination, TD OCT and SD OCT were performed. The following parameters were selected: Superior max, Inferior max, Superior average thickness, Average superior thickness, Average Foveal thickness from TD OCT and Average ganglion cell complex, superior ganglion cell complex, inferior ganglion cell complex, foveal loss ganglion cell complex, global loss ganglion cell complex, average full retina, superior full retina, inferior full retina, focal loss full retina, global loss full retina, average outer retina, superior outer retina, inferior outer retina, focal loss outer retina, global loss outer retina from SD OCT. Student’s t-test was used to compare the two sets of data when the distribution of the data was normal. Mann–Whitney test coefficient was utilized to compare the two sets of data when they did not follow a normal distribution. The statistical power of the study ranged between 76.2 and 94.2% with an alpha of 0.05 and a beta of 0.5. Bonferroni correction was applied to Student’s t-test because otherwise we would have a significant chance of 40.1% of our finding.

Results: In the affected eye group a reduction of the average thickness of retinal nerve fibre layer (RNFL) was found using TD OCT and the reduction was of 22.78% and the difference was statistically significant (P<0.001) between the two groups in almost all the investigated retina areas. Similar results were found when eyes were analysed with SD OCT, also when the ganglion cell layer (GCC) was considered: a reduction of 18.08% of GCC average thickness was found. No significant difference was found when the outer retina was considered.

Conclusions: In MS patients both OCT systems were able to detect differences between eyes with an outcome of optic neuritis and those without optic neuritis.

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Program Number: 5537 Poster Board Number: B0108
Presentation Time: 8:30 AM–10:15 AM

Intravitreal injection of erythropoietin in late-stage optic neuropathy
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Purpose: Recent clinical findings have showed that erythropoietin (EPO) has both neuroprotective and neuroregenerative capabilities for axonal degenerative disease of the optic nerve. In this retrospective interventional study, we evaluated if intravitreal EPO administration has any neuroregenerative effect in patients with late-stage optic neuropathy, or not.

Methods: Twelve eyes of 12 patients with optic atrophy [(defined as overall thinning (90 μm) in the retinal nerve fiber layer (RNFL)] from definite demyelinating optic neuritis history were included. Patients who had both minimum 6-months medical history and light perception vision in the affected eye, were enrolled into the study. Using pars plana approach, 2000IU/0.2ml EPO(Eprex:4000IU/0.4ml, Janssen-Cilag AG, Switzerland) was administered intravitreally with a 30-gauge needle on a tuberculin syringe. Injections were administered 3-times with 6-weeks intervals. Clinical: [Best corrected visual acuity (BCVA) and ophthalmoscopic and laboratory (OCT measurements, electrodagnostic tests)] examinations were repeated at regular intervals, and final visit was performed 3-months after the third intravitreal EPO injection. The primary outcome parameters, BCVA and RNFL thickness and secondary outcome parameters, visual evoked potentials (VEP) and electroretinography (ERG) at initially and at final visit were analyzed.

Results: No inflammatory, immunological or proliferative response was detected. The median BCVA of the patients with optic atrophy was 1.71±0.5-3.1 logMAR at initially and 1.69±0.5-3.1 logMAR at final visit. No one obtained minimum 0.2 logMAR BCVA improvement (success criteria). RNFL value was 49.1±22(22-88)μm before injections, and 48.6±20(25-81)μm after injections. The mean amplitude values of combined response in ERG(N35-P50, P50-N95) were 5.68±2(2.9-10.2)μV, 6.91±3(7.4,7.9)μmV before the injections and 5.45±2(2.6,9.6)μmV, 6.73±2(3.7-12)μmV after the injections, respectively. The mean amplitude and latency values of response in VEP 121.25±19.5(90-153)μm and 3.75±2(1.4,12)μmV before the injections and 114.8±15(93-134)μm and 3.96±3(0.7-12.4)μmV after the injections, respectively.

Conclusions: Intravitreal EPO injections has no neuroregenerative effect on the optic nerve when it was administered in the late period (>6months) of optic neuropathy. Meanwhile, we did not find any adverse effects of this administration on visual parameters and retinal microstructures.

Commercial Relationships: Bekir Kucuk, None; Uğur Acar, None; Koray Sevinc, None; Seçkin Aykas, None; Mesut Erdurmus, None; Gungor Sobaci, None.

Program Number: 5538 Poster Board Number: B0109
Presentation Time: 8:30 AM–10:15 AM

The design of a randomized clinical trial on the neuroprotective properties of erythropoietin in optic neuritis: Treatment of Optic Neuritis with Erythropoietin (TONE)
Wolf Lagrèze, Ricarda Diem. 1Ophthalmology, University of Freiburg, Freiburg im Breisgau, Germany; 2Neurology, University Heidelberg, Heidelberg, Germany.

Purpose: After successful completion of the VISION PROTECT pilot trial (NCT00355095) providing the first morphologic OCT-based evidence for neuroprotection with erythropoietin in optic neuritis, the German government has recently approved a subsequent, full-scale, nationwide randomized controlled clinical trial (NCT01962571), whose design we intend to present here.

Methods: A power analysis based on publications on the natural course and thinning of the peripapillary retinal nerve fiber layer after optic neuritis yielded a number of 47 patients in each treatment arm of a placebo-controlled, randomized, double-blind clinical trial to demonstrate a treatment effect of 50% reduction of nerve fiber loss with an α of 0.05 and β of 0.80.

Results: Recruitment of TONE has commenced in December 2014. Patients are randomized on either i.v. placebo or intravenous 33,000 IU i.v. erythropoietin as an add-on to a 3-day course of i.v. megadose methylprednisolone. Primary outcome measure is the peripapillary retinal nerve fiber layer thickness determined with the NSITE 6.0.
software of the Spectralis®-OCT. Secondary analyses comprise retinal layer segmentation. Functional measures are ETDRS-chart based visual acuity at 2.5% and 100% contrast, contrast sensitivity, volumetric analysis of the visual field defect determined by the German Adaptive Threshold Estimation (GATE) algorithm, VEP-latencies and vision-related quality of life. Results are expected after completion presumably in 2017. A 1.5 year open label follow-up shall provide further insights of erythropoietin effects with regard to MS-progression.

**Conclusions:** A positive outcome of the TONE-Trial would not only provide new treatment options for patients with optic neuritis, but might promote further clinical research in multiple sclerosis.

**Commercial Relationships:** Wolf Lagrèze, None; Ricarda Diem, None

**Support:** BMBF (German Ministry of Education and Research)

**Clinical Trial:** NCT01962571

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**Program Number:** 5539

**Poster Board Number:** B0110

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

**Early treatment of recombinant human granulocyte colony stimulating factor (G-CSF) in the rat model of anterior ischemic optic neuropathy (rAION) reveals a beneficial neuroprotective effect**

**Rong-Kung Tsai**†, ‡, Yao-Tzeng Wen†, Chung Hsing Chang†, †Institute of Eye Research, Buddhist Tzu-Chi Medical Center, Hualien, Taiwan; ‡Institute of Medical Sciences, Tzu Chi University, Hualien, Taiwan; †Department of Dermatology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

**Purpose:** Our previous report demonstrated that immediate administration of recombinant human granulocyte colony-stimulating factor (G-CSF) had neuroprotective effects in a rat model of anterior ischemic optic neuropathy (rAION). This study is aimed to investigate whether delayed treatment of G-CSF is as effective as early treatment after rAION induction.

**Methods:** The rAION rats were subcutaneously injected G-CSF starting at day 0, 7, and 14-post rAION induction for 5 consecutive days. Survival rate of retinal ganglion cells (RGCs) was determined by using retrograde labeling of Fluorogold. Apoptosis in RGCs layer and inflammation at optic nerve (ON) were measured by TUNEL assay and immunohistochemical (IHC) staining of ED1 respectively. Visual function was assessed by photopic flash visual evoked potentials (FVEP).

**Results:** G-CSF treatment started at day 0-post rAION induction had significant better survival rate of RGCs than treatments at day 7 and 14-post infarct both in central and mid-peripheral retinas (p<0.05). Treatment with G-CSF at day 0-post rAION induction resulted in significantly lower number of apoptotic cells in RGCs layer of retinas and significantly lower level of inflammation at ON than treatment at day 7 and 14-post rAION induction (p<0.05). Rats received G-CSF treatment at day 0-post rAION induction preserved better latency and amplitude of the p1 wave in FVEP than rats treatment with G-CSF at day 7 and 14-post rAION induction (p<0.05).

**Conclusions:** Early treatment with G-CSF has significantly better neuroprotective effects on RGCs and optic nerve than the delayed treatment starting at 1 or 2 weeks post-infarct.

**Commercial Relationships:** Rong-Kung Tsai, None; Yao-Tzeng Wen, None; Chung Hsing Chang, None

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**Program Number:** 5540

**Poster Board Number:** B0111

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

**The Presence of Calcium Significantly Enhanced Annexin-V-Labelling of Degenerating Axons after Experimental Anterior Ischemic Optic Neuropathy**

Gun Ho Lee†, M Ali Shariati†, Ming-Hui Sun‡, †Taiwan; †Stanford University, Cupertino, CA; ‡Chang Gung Memorial Hospital - LinKou, LinKou, Taiwan.

**Purpose:** Annexin-V binds to exposed phosphatidylserine on the extracellular membrane in a calcium-dependent fashion and has been shown to label degenerating retinal ganglion cell axons and soma after experimental anterior ischemic optic neuropathy (AION). Because the labeling of degenerating axons with annexin-V is relatively labile, in this study, we determine whether inclusion of calcium in different experimental steps helps to enhance axonal labeling.

**Methods:** We induced optic nerve head ischemia in adult C57BL/6 mice using laser-assisted photochemical thrombosis. After one week, we performed intravitreal injection of annexin-V-A488 and imaged the retina 2-3 hours later using confocal scanning laser ophthalmoscopy (cSLO) and optical coherence tomography (OCT). Then, we prepared retinal whole mount in calcium-free or 2.5 mM CaCl₂ conditions and imaged the retinae using fluorescence microscopy for up to 7 days after mounting.

**Results:** On the day of annexin-V-A488 labeling, degenerating axons were easily seen in both Ca²⁺-containing (N = 30) and Ca²⁺-free (N = 10) conditions. Annexin-V-A488 labeling of degenerating axons one week after ischemia correlated well with the presence of optic nerve swelling on day-1 as measured by OCT. No annexin-V-A488 labeling of axons was seen in the control eyes (N = 6), which showed no swelling on OCT. Inclusion of Ca²⁺ to the fixative, wash, and mounting solutions significantly improved the persistence of annexin-V-A488 signal one to seven days after labeling. In contrast to the difficulty of preserving axonal labels, bright annexin-V-A488 signal on degenerating soma was easily seen even one week after labeling. We used these brightly labeled soma to test the lability of annexin-V-A488 labeling over 5, 10, and 20 min of light exposure and found a dramatic, time-dependent decrease in fluorescence signal, consistent with the relative lability of the annexin-V-A488 signal.

**Conclusions:** Annexin-V-A488 brightly labels degenerating retinal ganglion cell axons one week after experimental anterior ischemic optic neuropathy, and the presence of 2.5 mM Ca²⁺ during retinal tissue preparation helps preserve this relatively labile label. During microscopy, even minutes of bright light exposure can quench annexin-V-A488 signal, and every effort should be made to shield the tissue from bright light during experimentation.

**Commercial Relationships:** Gun Ho Lee, None; M Ali Shariati, None; Ming-Hui Sun, None; Yaping J. Liao, None

**Support:** Stanford Undergraduate Advising and Research Grant, Vice Provost for Undergraduate Education Grant

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**Program Number:** 5541

**Poster Board Number:** B0112

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

**Rapamycin rescues the innate immune/inflammatory response in the retina of the Ndufs4 mouse**

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**Purpose:** Mitochondrial complex I dysfunction has been shown to lead to vision loss via the loss of function of retinal ganglion cells (RGCs), however the mechanism of which that occurs is unclear. A recent study has shown that rapamycin treatment of Ndufs4
deficient mice alleviates mitochondrial disease and prolongs the life expectancy of these mice by reducing mTOR signaling. The goal of this study is to see the effects of rapamycin treatment in the retina of these mice by evaluating innate immune and inflammatory transcripts that we have already seen to increase in the Ndufs4 KO mouse. This will be valuable in developing therapeutics for mitochondrial visual diseases, such as Leber’s hereditary optic neuropathy (LHON) and Autosomal dominant optic atrophy (ADOA).

**Methods:** Two Ndufs4 KO and two wild type controls received intraperitoneal injection (IP) of rapamycin (8mg/kg) daily for nine days starting from P22. Additionally, two Ndufs4 KO and two wild type controls received IP injection of vehicle. Experiments were conducted in compliance with the ARVO Statement for the Use of Animals in Ophthalmic and Visual Research. After nine days of treatment the mice were sacrificed and the retinas were surgically removed and placed in RNALater. Total RNA was extracted from the retinas and cDNA was synthesized for evaluation by qRT-PCR. The primers tested include: Fas, Tlr4, Ccl5, Ccl12, C1ra, Tlr3, Mmp12, Icam1, Cxcl9, Aif1, Tlr2, Cd68, C1qc, B2m, and Cxcl10. Analysis was done by calculating the delta delta Ct and statistical significance was determined by student’s t-test (2 tailed; equal variance).

**Results:** Of the inflammatory transcripts tested, 16 out of 16 transcripts showed mean elevation compared to wild type controls, as was previously seen. Treatment with rapamycin inhibited the inflammatory response and the mean levels of all 16 transcripts rebounded and returned to values similar to wild type controls, as was previously seen. Treatment with rapamycin rescues this innate immune and inflammatory response. Systemic treatment with rapamycin rescues innate immune and inflammatory response and may prevent RGC death-mediated vision loss. This will provide therapeutic insight in mitochondrial diseases such as LHON and ADOA.

**Conclusions:** In the Ndufs4 retinal, mitochondrial complex I deficiency leads to vision loss, which is mediated by an innate immune and inflammatory response. Systemic treatment with rapamycin rescues innate immune and inflammatory response and may prevent RGC death-mediated vision loss. This will provide therapeutic insight in mitochondrial diseases such as LHON and ADOA.

**Commercial Relationships:** Alfred K. Yu, None; Lanying Song, None; Karl Murray, None; Gino Cortopassi, None

**Support:** NH Grant EY012245

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**Lucentis is Not Neuroprotective in a Primate Model of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)**

**Mary A. Johnson**, Neil R. Miller, Steven L. Bernstein, 'Ophthalmic and Vis Science, Univ of Maryland Sch of Medicine, Baltimore, MD; 2Ophthalmology, Johns Hopkins Univ. Sch. Med., Baltimore, MD.

**Purpose:** Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) is the most common cause of acute optic nerve-related vision loss in people over 50. There is no treatment. A retrospective study (Saati et al., 2013) and 2 small case studies (Bennett et al., 2007; Bajin et al., 2011) suggested that a single intravitreal (IVT) injection of ranibizumab protects against vision loss in NAION. A Genentech-supported clinical trial was completed in 2012; the results have not been announced. The relatively rare nature of the disorder and the 40% incidence of spontaneous improvement (IONDT, 1995) are challenges for NAION clinical studies. For this reason, we tested the efficacy of a single IVT injection of ranibizumab (Lucentis) in our primate model of NAION (pNAION).

**Methods:** Four normal male rhesus monkeys (8 - 12kg) were given a single IVT injection of Lucentis (1.25mg in 0.05ml) immediately following induction of experimental NAION (Chen & Johnson et al., 2008) in one eye. Four weeks later the fellow eye was induced and injected with a single IVT dose of vehicle. Spectral-domain OCT (Heidelberg, Inc), flash electroretinograms (ERGs), and simultaneous pattern ERG (pERG) and pattern visual evoked potentials (VEPs) were recorded, and fundus photography and fluorescein angiography (FA) were performed on each animal before and at 1 day, 1 week, 2 weeks, 4 weeks and 8-12 weeks after induction of pNAION. Animals were sacrificed within 2 weeks of final assessment. Differences in the retinal ganglion cell (RGC) numbers in each eye were estimated by stereological analysis of optic nerve axons. Optic nerve axons, myelin and inflammatory cells were evaluated using immunohistochemistry.

**Results:** Lucentis conferred no advantage to the treated eye in development or resolution of macular (p = 0.45) or peripapillary
edema (by OCT), in retention of VEP (p = 0.19) and pERG (p = 0.28) amplitudes, in the time course of optic nerve leakage and fluorescein dye staining, or in preservation of RGCs, compared with vehicle controls. Three of the 4 Lucentis-treated eyes showed more peripapillary leakage and eventual atrophy than the vehicle-treated eyes.

Conclusions: IVT administration of Lucentis showed no evidence of neuroprotection in a primate model of NAION, despite maximal dosing and immediate treatment post-induction. This finding suggests that VEGF inhibition is likely to be ineffective in clinical NAION treatment.

Commercial Relationships: Mary A. Johnson, None; Neil R. Miller, None; Steven L. Bernstein, None
Support: NIH Grant EY019529

Program Number: 5544 Poster Board Number: B0115
Presentation Time: 8:30 AM–10:15 AM
Characterization and application of a nonhuman primate model of non-arteritic anterior ischemic optic neuropathy for therapeutic screening
Matthew S. Lawrence1, Jordan Attwood1, Alex Lewis1, Rohn Brookes1, Vernard Woodley1, Meghan Tucker1, Wenzheng Hu1, Robin J. Goody1, Sean Callanan1, Demetrios Vavvas1; 1Research, RxGen, Hamden, CT; 2Ross University, Basseterre, Saint Kitts and Nevis; 3Massachusetts Eye and Ear Infirmary, Boston, MA.

Purpose: To characterize the nature and time course of optic nerve and retinal pathology following induction of non-arteritic anterior ischemic optic neuropathy (NAION) by focal phototherapeutic insult to the optic nerve head (ONH) in African green monkeys, and to evaluate the effect of candidate neuroprotective agents in reducing the elicited pathology.

Methods: Fifteen adult monkeys received unilateral ONH laser treatment (wavelength 532nm; power 100mW; spot size 500mm; duration 9 seconds x 4), immediately following intravenous administration of rose bengal (0.1 ml/kg of 25 mg/kg) to induce oxidative endothelial injury of ONH microvasculature. Eyes were evaluated by slit lamp exam, color fundus photography, fluorescence angiography, optical coherence tomography (OCT) and electroretinography (ERG) at baseline and days 1, 7, 14, 28, 56 and 84 post-laser. Apoptosis and necrosis inhibitors or vehicle were administered intravitreally immediately following laser treatment.

Results: Phototherapeutic injury to the ONH employing the applied laser parameters consistently triggered the onset and evolution of a pathology very similar to clinical NAION, with ONH edema within 24 hours, followed by retinal venous stasis, peripapillary hemorrhages, and optic nerve fiber layer (ONFL) thickening over the ensuing week, which gradually resolved, leaving residual ONH pallor and ONFL thinning. Electrophysiological changes were correlated with ONFL changes detectible by OCT. Terminal histology findings were additionally correlated with in-life exam findings. Intervention with pan-caspase and receptor interacting protein 1 kinase inhibitors at the doses explored positively modulated endpoints, although demonstration of statistically significant therapeutic effect was limited by sample size.

Conclusions: Phototherapeutic NAION in the green monkey exhibits pathological changes very similar to the human condition with early onset ONH and retinal edema followed by ONFL thinning with associated ERG changes indicative of functional deficit, all of which can be evaluated in a quantitative, longitudinal manner. This supports application of the model as a test system to further understand the pathophysiology of NAION and the evaluation of candidate therapies, the utility of which has been demonstrated in our initial exploration of the therapeutic effect of cell death pathway inhibitors.

Commercial Relationships: Matthew S. Lawrence, RxGen (F); Jordan Attwood, RxGen (F); Alex Lewis, RxGen (F), RxGen (F); Rohn Brookes, RxGen (F); Vernard Woodley, RxGen (F); Meghan Tucker, RxGen (F); Wenzheng Hu, RxGen (F); Robin J. Goody, RxGen (F); Sean Callanan, None; Demetrios Vavvas, None
Support: NEI 1 R43 EY023867-01

Program Number: 5545 Poster Board Number: B0116
Presentation Time: 8:30 AM–10:15 AM
Risk factors associated with nonarteritic anterior ischemic optic neuropathy in young patients at a reference center in Mexico City
SECTION: Eye Movements/Strabismus/Amblyopia/Neuro-ophthalmology (EY)
Mariana A. Flores, Laura Andrea Torrado, Mayra F. Camargo. Ophthalmology, Instituto de Oftalmologia, Mexico City, Mexico.

Purpose: Nonarteritic anterior ischemic optic neuropathy remains a diagnosis for people older than 50 years old. We aim to describe the demographic characteristics and risk factors associated with nonarteritic anterior ischemic optic neuropathy in patients younger than 50 years old in a reference center in Mexico City.

Methods: Retrospective analysis of the medical records of all the patients diagnosed with nonarteritic anterior ischemic optic neuropathy from September 2007 to November 2014 in a reference center in Mexico City. We include age, sex, best-corrected visual acuity and comorbidities associated. We exclude those patients with an incomplete record.

Results: We found 1967 medical records with the diagnosis of nonarteritic anterior ischemic optic neuropathy. 177 patients were younger than 50 years old (ranged: 2-49 years-old). 110 females 67 males. 23.16% presented dyslipidemia (41 patients), 22.60% with diabetes mellitus type 2 (40 patients) and 19.77% primary systemic hypertension (35 patients). Thirteen patients (7%) presented with a history of trauma, 4.51% (8 patients) with hemorrhagic or ischemic cerebral vascular event and 2.8% with a cerebral tumor (5 patients).

In the group of patients younger than 30 years old a repetitive antecedent of neonatal hypoxia was found (12 patients, 6.7%) and only one case with hereditary optic neuropathy.

Conclusions: In this study we found that the comorbidity such as dyslipidemia, diabetes mellitus and hypertension represented the most significant risk factors for presenting with nonarteritic ischemic optic neuropathy. This is the first information obtained in Latin American population. We believe that the Mexican diet and lifestyle could have an important impact in its development and more studies need to be done.

Commercial Relationships: Mariana A. Flores, None; Laura Andrea Torrado, None; Mayra F. Camargo, None

Program Number: 5546 Poster Board Number: B0117
Presentation Time: 8:30 AM–10:15 AM
50% of Non-Arteritic Anterior Ischemic Optic Neuropathy Occurs between 40–55 Years Old
Ming-Hui Sun1, Yaping J. Liao1, M Ali Shariati1. Ophthalmology, Byers Eye Institute Stanford University, Palo Alto, CA; 3Ophthalmology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan; 4Ophthalmology, Stanford University School of Medicine, Palo Alto, CA.

Purpose: Non-arteritic ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in those older than 50. and young onset NAION has been reported in 4.23% of patients. The aim of our study is to investigate the age of onset of NAION and correlation with risk factors.

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Methods: We performed a retrospective review at a single institution of consecutive patients with the diagnosis of NAION (2009-2014) who had neuro-ophthalmic evaluation, automated static perimetry, and optical coherence tomography (OCT).

Results: We studied 50 NAION eyes in 32 patients (24 male, 8 female; unilateral: 14 patients, bilateral: 18 patients). The average age of first events was 54.6±2.4 years (median 54 years; ≤50: 11 (33.7%) patients, >50: 20 (66.3%) patients; range 24-80 years). In fact, 50% of patients presented with their first event between ages 40-55. In all ages, AION led to significant visual field loss (mean deviation AION: -1.1±1.5 dB; control: -1.6±0.5 dB; P<0.001, Mann-Whitney) and significant thinning of thickness of the retinal nerve fiber layer (AION: 66.0±3.9 μm; control: 89.9±4.6 μm; P<0.001) and macular ganglion cell complex as measured by OCT (AION: 61.7±1.8 μm; control: 82.4±3.4 μm, P<0.001). In terms of AION risk factors, all age groups had small optic disc area (mean optic disc area 1.65 ±0.30 mm², N = 43 eyes), obstructive sleep apnea (≤50: 82%, average AHI 27.9±7.9; >50: 80%, average AHI 24.6±7.7), and vascular risk factors (hypertension, diabetes, hyperlipidemia). Treatment for obstructive sleep apnea did not prevent future events but was associated with delayed onset of new events (treated: 63.5±54.9 months, median 10 months; not treated: mean 21.6±16.4 months, median 5 months; P=0.2). The presence of optic disc drusen was associated with earlier onset of AION by 2 decades (N=2 patients, 3 affected eyes), but all affected eyes had final visual acuity of 20/20. Consistent with this finding, age may be an important factor in visual prognosis, since those ≤50 years old at first event had a trend of better final visual acuity, visual field mean deviation, and OCT retinal thickness measurements than those >50.

Conclusions: Fifty percent of NAION patients had onset of first event at 40-55, so age greater than 40 should be considered the common presentation of NAION. Age may also be an important factor in NAION prognosis, since younger patients had better visual outcome.

Commercial Relationships: Ming-Hui Sun, None; Yaping J. Liao, None; M Ali Shariati, None

Program Number: 5547 Poster Board Number: B0118
Presentation Time: 8:30 AM–10:15 AM

Nocturnal Diastolic Blood Pressure decrease under 50mmHg is a risk factor for Nonarteritic Anterior Ischemic Optic Neuropathy in elderly patients

thibaut Chapron1, 2, Fouzia Mantout, Sylvie Feldman, marie helene errera1, Laurence Du Pasquier1, Isabelle Rossignol1, Rabah Benrabah1, Emmanuel Heron1.

1Internal medicine, Hospital Quinze Vingt, Paris, France; 2Université Paris Descartes, Paris, France; 3Univerité Paris Descartes, Paris, France; 4Ophthalmology 4, Hopital Quinze Vingt, Paris, France.

Purpose: To analyze 24-hours Arterial Blood Pressure (ABP) recordings in elderly patients with Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) compared with other retinal vascular diseases.

Methods: Over a 7-year period, 49 NAION patients and 27 control subjects with sudden visual loss due to arterial, venous or diabetic retinal vascular acute episodes, all aged 70 or more, underwent 24-hours ABP recordings. Our main outcome was the number of patients with one or more nocturnal diastolic ABP fall under 50 mmHg. Number of patients with one or more nighttime systolic ABP fall under 90 mmHg, mean systolic and diastolic ABP during 24-hours, daytime and nighttime, as well as standard NAION risk factor were also studied.

Results: Nocturnal diastolic ABP values ≤50 mmHg were observed in 20 (41%) NAION and 4 (15%) control subjects (P=0.02), Nocturnal systolic ABP values ≤90 mmHg were observed in 5 (10%) NAION and 4 (15%) control subjects (p=0.55). Mean systolic(SD)/diastolic(SD) 24-hour ABP was 134(17)/70(9) mmHg in NAION and 135(20)/71(10) mmHg in control subjects (P=0.78). No statistically significant difference was observed regards of mean systolic and mean diastolic ABP whether in daytime or nighttime recordings. 23 (46%) NAION and 19 (70%) control subjects took hypotensive drug therapy (p=0.04). Sex ratio, body mass index, and the frequency of diabetes and dyslipidemia were not different.

Conclusions: Nocturnal diastolic ABP fall under 50mmHg, a risk factor for cerebral hypoperfusion, is significantly more frequent in elderly patients with acute visual loss due to NAION compared with other vascular retinal etiologies, and appears to be a specific risk factor for this disease.

Commercial Relationships: thibaut Chapron, None; Fouzia Mantout, None; Sylvie Feldman, None; marie helene errera, None; Laurence Du Pasquier, None; Isabelle Rossignol, None; Rabah Benrabah, None; Emmanuel Heron, None

Program Number: 5548 Poster Board Number: B0119
Presentation Time: 8:30 AM–10:15 AM

MMP19 Expression in the Human Optic Nerve

Ralph Hazlewood1, 2, Kathy Miller1, 2, Robert F. Mullins1, 2, Markus H. Kuehn1, 2, Lee M. Jampol3, John H. Fingert1, 2.

1Ophthalmology and Visual Sciences, University of Iowa, Iowa City, IA; 2Stephen A. Wynn Institute for Vision Research, Iowa City, IA; 3Ophthalmology, Feinberg School of Medicine, Northwestern University, Chicago, IL.

Purpose: We previously linked MMP19 mutations with a congenital malformation in which the optic disc is deeply excavated known as cavitary optic disc anomaly (CODA). The purpose of this study was to investigate the expression of MMP19, a secreted matrix metalloproteinase, within the optic nerve.

Methods: MMP19 protein expression in the optic nerve was evaluated by immunohistochemistry in sagittal and en face sections of optic nerves obtained from normal human donor eyes. Sections were co-labeled with antibodies directed against glial cells (GFAP), ganglion cell axons (βIII Tubulin), and microglia (CD45). All experiments were conducted in triplicate using three different human donor eyes.

Results: MMP19 immunolabeling was observed throughout the optic nerve including the optic nerve head. Expression was highest in the prelaminar region and lamellar region, with much lower levels in the retrolaminar region. Differential MMP19 labeling was also observed in the cross-sections of the optic nerve, with increased signal in the periphery or edges towards the scleral canal and pia mater. Additionally, no significant co-localization was observed between MMP19 and markers of glial cells, ganglion cell axons, or microglia.

Conclusions: Immunohistochemical analysis shows that MMP19 is strongly expressed in the optic nerve head of human donor eyes, the primary site of pathology in CODA patients. No obvious co-localization was observed with markers for cell types that populate the optic nerve, suggesting that MMP19 accumulates primarily within extracellular spaces in the optic nerve. Moreover, the lateral localization of MMP19 within the optic nerve suggests that dysregulation of its enzymatic function might undermine the adhesion between the optic nerve and the scleral canal and promote formation of an excavated optic nerve head – the key feature of CODA.

Commercial Relationships: Ralph Hazlewood, None; Kathy Miller, None; Robert F. Mullins, None; Markus H. Kuehn, None; Lee M. Jampol, None; John H. Fingert, None

Support: NIH (Grants R21 EY24621, R01EY018825, R01EY023512) to J.H.F and the Dean’s Graduate Fellowship, the University of Iowa to R.J.H.
Purpose: The rat optic nerve axons come from the retinal ganglion cells. Only a few of them have their origin in the prectental area. The diameters of the optic nerve axons are far from being a homogeneous population. There are at least three main groups of ganglion cells in rat retinas and three different axon types in the rat optic nerve. The morphometric study of optic nerve fibers is a useful tool to research the function, development, aging and pathologic conditions of them. Thus, classification of the optic nerve axons is crucial in order to make experimental comparisons. The aim of this work is to classify the optic nerve axons by analyzing their ultrastructural parameters with Artificial Intelligence (AI) methods.

Methods: Adult albino Wistar rats were anesthetized, transectarily perfused and its optic nerves removed and processed for ultrastructural microscopy studies. Optic nerve axons were analyzed with a computer-linked planimeter. Several parameter, were obtained for each axonal cross-section using a computer program. The parameters were: axon diameter, axon area, myelin sheath thickness, G-Ratio, microtubule number (MTn), neurofilament number (NFn) and R-proportion (R = NFn/[NFn+MTn]). Data were processed with a set of AI methods, two supervised techniques, Multilayer Perceptron (MLP) and Decision Trees (DT), and other unsupervised one, K-Means clustering. All the computations of the decision tree were developed using the WEKA software (Machine Learning Group at the University of Waikato).

Results: Using k-means clustering analysis we were able to identify three different groups of fibers in the optic nerve, which are consistent with the results obtained in functional studies. The main parameters that allowed us the classification of optical nerve fibers were axon diameter, G-Ratio, and R-proportion. Using these parameters, we analyzed the classification accuracy of MLP and DT, as tools to develop an automated system. In both cases, the classification Accuracy was above 95%, being higher with the MLP technique that reached a 98.9% of accuracy.

Conclusions: Results show that morphometric parameters can be used to identify different populations of nerve fibers, with a high accuracy when AI methods are used. Only a limited number of parameters are needed to produce a consistent classification. The MLP technique is the most useful.

Commercial Relationships: Joaquin De Juan, None; Jose L. Girela, None; David Gil, None; Noemi Martinez-Ruiz, None; Jorge Azorin, None; Bassima Boughlala, None

Support: Vicerrectorado de Innovación, University of Alicante, Spain (Vigrob-137)

Program Number: 5550 Poster Board Number: B0121
Presentation Time: 8:30 AM–10:15 AM

Lamina Cribrosa Position Changes with the Valsalva maneuver Keegan Harkins, Sachin Kedar, Yasir J. Sepah, Mohammad A. Sadiq, Justin West, Deepta Ghate. 1Ophthalmology, University of Nebraska Medical Center, Omaha, NE; 2College of Medicine, University of Kentucky, Lexington, KY.

Purpose: The Valsalva maneuver (VM) causes an increase in intraocular pressure (IOP) and intracerebral pressure (ICP). This prospective clinical study aimed to test if acute changes in ICP and IOP can cause changes in the lamina cribrosa (LC) position.

Methods: The study population had 20 healthy volunteers from the University of Kentucky. VM was performed with a manometer and a mouth pressure of 30-33 cm of H2O held for 15 seconds. The Icare® tonometer was used to check IOP before and during the VM (after 15 seconds). The Spectralis OCT® was used to acquire 12 radial optic nerve head images before and during the VM (after 15 seconds). There was a 10 minutes gap between right and left eye measurements and between the IOP and OCT acquisition. 3 of the 12 radial OCT sections (selected by expert grader) were independently graded by 2 graders for anterior lamina cribrosa depth (LCD), Bruch’s membrane opening width (BMO) and cup depth from BMO plane. Any image with a measurement discrepancy>40 μm was re-graded by the expert grader.

Results: The mean age was 29±4.7 years with 40 eyes analyzed. There was no significant change in BMO depth (mean change -3.7±37.5 μm), cup depth (mean change -1.3±24.1 μm) and LC depth (mean change -0.3±31.4 μm) with the VM. IOP increased with the VM in all eyes (mean change 3.2±2.2 mmHg, p<0.05). 20 eyes had anterior LC shift with the VM (mean LC position change -20.9±13.6 μm). 14 eyes had LC posterior shift (mean LC position change -29.2±28.2 μm). 2 eyes had no change in LC position and 4 eyes had ungradable LC. Mean IOP change was significantly (p<0.05) higher with anterior LC shift (3.65 mm Hg) versus posterior LC shift (2.93 mm Hg). There was no significant difference in IOP change with BMO widening versus shortening and in anterior and posterior cup depth shift. There was no significant association between BMO widening or shortening or anterior or posterior LC shift. There was a significant association between anterior and posterior shift of the LC and cup depth (chi square = 4.37, p=0.05).

Conclusions: Despite an IOP rise in all eyes, the VM causes anterior LC shift in 50% of eyes. This anterior LC shift is associated with higher IOP change and an anterior shift of the cup depth but not with BMO width changes. The eyes with anterior LC shift presumably had a rise in IOP> IOP which would presume that the LC position changes with fluctuations in ICP.

Commercial Relationships: Keegan Harkins, None; Sachin Kedar, None; Yasir J. Sepah, None; Mohammad A. Sadiq, None; Justin West, None; Deepta Ghate, None

Program Number: 5551 Poster Board Number: B0122
Presentation Time: 8:30 AM–10:15 AM

Color-Fundus-Feature-Based Prediction of Regional SD-OCT-Based ONH-Volume in Optic Nerve Edema Jason Agne1, Jui-Kai Wang2, Randy H. Kardon3, 3, Mona K. Garvin1, 1.

1Department of Electrical and Computer Engineering, The University of Iowa, Iowa City, IA; 2Department of Biomedical Engineering, Iowa City VA Health Care System, Iowa City, IA; 3Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA.

Purpose: Optic nerve edema is commonly assessed via direct funduscopic observation or digital fundus photographs using a six-stage Frisen grading scale. While 3D image-analysis of spectral-domain optical coherence tomography (SD-OCT) can provide volumetric measures of optic nerve head (ONH) swelling (Wang et al., IOVS 2012), developing automated objective quantitative measures of the degree of swelling is important in situations where SD-OCT is not commonly available, such as in emergency rooms. The purpose of this work is to develop and evaluate a machine-learning approach for the prediction of regional SD-OCT volumetric measures from color-fundus-photographic features.

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Methods: Our previously developed 3D image-analysis approach was used to measure regional (nasal, superior, temporal, and inferior regions within 1.73 mm of the center of the ONH) from 48 ONH-centered SD-OCT volumes (Zeiss Cirrus) of 48 patients with varying stages of optic nerve edema (Figure 1a,b). Features concerning the boundary of the ONH swelling (such as the area of the bounded region and the smoothness of the boundary), global and local texture features (such as joint entropy of various image transformations and local entropy of the area bounded by the ONH swelling), and vessel features (such as edge derivative values, and a measure of vessel discontinuity) were extracted from color fundus photographs taken on the same day (Figure 1c) using our automated approach, and used in a leave-one-patient-out random forest regression to predict the volumetric information for each region of the SD-OCT image.

Results: Pearson correlation coefficients of $R_{nasal} = 0.74$, $R_{superior} = 0.66$, $R_{temporal} = 0.68$, and $R_{inferior} = 0.67$ were obtained between our fundus-based predicted measures and the actual SD-OCT-based regional measures. Scatter plots are shown in Figure 2.

Conclusions: Regional 3D volumetric information can be predicted from 2D fundus information and demonstrates the feasibility of objectively and quantitatively measuring optic nerve edema from fundus photographs alone.

From top to bottom: (a) Example 3D rendering of top surface from SD-OCT image with the primary region indicated. (b) Computed volumetric measures of ONH displayed on a thickness map. (c) Corresponding fundus image.
The volume for each sub-region as predicted from this method plotted against the volume for each sub-region as computed with a segmentation of SD-OCT images.

**Commercial Relationships:** Jason Agne, None; Jui-Kai Wang, None; Randy H. Kardon, Acorda (C), Department of Veterans Affairs Research Foundation, Iowa City, IA (S), Fight for Sight Inc (S), Novartis (C); Mona K. Garvin, The University of Iowa (P)

**Support:** R01 EY023279

**Program Number:** 5552 Poster Board Number: B0123

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

**Multifocal Photopic Negative Response (mfPhNR) and Central Lineal Visual Sensitivity in Patients with Optic Nerve Lesions Ari Kamei1, Eiichiro Nagasaka2. 1Ari Eye Clinic, Oshu-Mizusawa, Japan; 2Mayo Corp., Inazawa, Japan.

**Purpose:** To evaluate the interrelation of mfPhNR and Central Lineal Visual Sensitivity in superior and inferior in patients with optic nerve lesions.

**Methods:** Thirteen eyes of thirteen volunteers with normal vision and eighteen eyes of nine patients with optic nerve lesions including normal tension glaucoma (NTG) were tested.

The mfPhNR was recorded with the VERIS Science System 5.0.4. The visual stimulus was made up of 37 hexagons in an approximately 40-degree visual field, Pseudo-randomly alternating between black (5cd/m2) and white (200cd/m2) on the CRT monitor. Burian-Allen ERG Electrodes, Adult-bipolar or Pediatric-bipolar, were used for this testing. The recording time was approximately 8 min. with dilated pupils having the best-corrected visual acuity. The band pass filter of the amplifier was set from 1 to 100 Hz. The amplification and stimulus frequency were set to 10000 and 9.41 Hz (8 frames) respectively.

Each trace of the mfPhNR found in superior and inferior regions was analyzed in about 10 degrees.

The static visual field was examined with a central 30-2 SITA Standard program using a Humphrey Field Analyzer. The mean deviation (dB) in 10 degrees was converted to lineal visual sensitivity (1/Lambert) to apply for the analysis.

**Results:** There was a correlation between the amplitude of the mfPhNR and Central Lineal Visual Sensitivity in the inferior (R=0.456, P=0.012). On the other hand, there was no correlation between the amplitude of the mfPhNR and Central Lineal Visual Sensitivity in the superior (R= 0.332, P= 0.068).

**Conclusions:** We presented previously that there was a strong correlation between the amplitude of mfPhNR and Lineal Visual Sensitivity in about 20 degrees. There was less correlation between the amplitude of mfPhNR and Lineal Visual Sensitivity in about 10 degrees.

**Commercial Relationships:** Ari Kamei, None; Eiichiro Nagasaka, None

**Program Number:** 5553 Poster Board Number: B0124

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

**OPTIC ATROPHY IN CLASSICAL METHYLMALONIC ACIDEMIA**

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**Purpose:** Methylmalonic acidemia (MMA) is an autosomal recessive disorder resulting in failure to process various amino acids and lipids. The classical form results in methylmalonyl CoA mutase deficiency, preventing the Vit B12-dependent conversion of methylmalonyl CoA to succinyl CoA, required in Krebs cycle. Patients typically present in early infancy with lethargy, vomiting, dehydration and failure to thrive. Long-term complications include renal failure (CRF), encephalopathy and pancreatitis. 4 cases of optic atrophy (OA) have been reported in classical MMA on appropriate dietary restrictions. The exact etiology is unknown but likely is multi-factorial. With improved survival of patients offered advanced treatment, OA needs to be identified so that prophylactic/therapeutic intervention, when available, can be incorporated into management protocols. The purpose of this observational study is to identify and determine the prevalence of OA in a small cohort of patients with classical MMA.

**Methods:** 22 patients clinically diagnosed and genetically confirmed to have classical MMA were assessed with full history, neuroophthalmic exam, fundus photos and visual evoked potentials (VEP). Diagnosis of OA was determined by a combination of visual acuity, pupil reactions, optic nerve appearances, OCT and VEP. Associations of tabulated data were determined using Mann-Whitney U, Kruskal-Wallis, Chi-squared and Fisher’s exact tests. Statistical significance was set at p<0.05. Patients with propionic acidemia and intracellular cobalamin metabolism disorders, which have clinical features of MMA were excluded.

**Results:** 8 patients were female and 14, male. Age range was 7 to 27yrs (median=14;IQR=11-16). 13 patients (59%) had OA; 85% of these were bilateral. 6 (46.15%) reported decreased vision and 7 (53.85%) were asymptomatic. 12 patients had CRF (median=16;IQR=14.5-20). Age was not significantly associated with OA (p=0.17) but significantly related to CRF (p=0.0067). Patients with OA were more likely to have CRF than those without OA (p=0.0058).

**Conclusions:** Optic atrophy is a frequent finding in classical MMA and most commonly is bilateral and sub-clinical. A positive correlation with CRF, known independently to be associated with...
OA, suggests a contributing causal relation. These findings have important clinical and management implications: early and periodic ophthalmic exams including VEP and OCT should be performed in all, including asymptomatic patients with MMA.

**Conclusions:** Optic nerve atrophy is a well-known feature of mitochondrial disease. Many mechanisms for the pathogenesis of mitochondrial optic neuropathy have been proposed including bioenergetic failure, oxidative stress and glutamate toxicity. The atrophy in MMA patients presents primarily in the superior and inferior quadrants of the optic nerve as measured by OCT which differs from other optic neuropathies. It is recommended that patients undergo regular eye examinations, including OCT to monitor for changes in retinal nerve fibers. Future studies with OCT measurements may help shed light on changes that occur over time as well as highlight the earliest signs of change and a potential therapeutic window in this disease process.

**Commercial Relationships:** Laryssa Huryn, None; Irini Manoli, None; Elizabeth Harrington, None; Jennifer Sloan, None; Brian P. Brooks, None; Charles Venditti, None; Wadih M. Zein, None

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**Program Number:** 5555 Poster Board Number: B0126

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

**Optic nerve morphology as a marker for disease severity in cerebral palsy of perinatal origin**

Deepta Ghate, Veda Vedanarayanan, James Corbett, Abdulbaset Kamour, Sachin Kedar.

**Purpose:** It has been hypothesized that a large cup in premature children is associated with period of gestation (POG) > 28 weeks. Early prognostication in children with POSE will result in early rehabilitation with improved functional outcomes. Recognition of the association of POSE and large cups will prevent unnecessary examinations under anesthesia for glaucoma. Our study aims to correlate optic nerve head (ONH) pallor and cupping to period of gestation (POG) at birth and severity of neurological damage in children with perinatal onset static encephalopathy (POSE).

**Methods:** 54 consecutive patients with POSE were enrolled. Exclusion criteria included genetic, metabolic or congenital structural brain abnormalities not related to perinatal complications; intracocular disease (ROP/glaucoma/cataract) and hydrocephalus. ONH morphology (pallor and cup to disc ratio-CDR) was assessed independently by 2 fellowship-trained ophthalmologists by dilated examination using direct and indirect ophthalmoscopy. ONH were labeled as pale or large cup (cup/disc ratio ≥ 0.5) only if the 2 ophthalmologists agreed. Inter-rater reliability was >0.8 for all parameters. A pediatric neurologist determined eligibility, age of onset of POSE, neurological deficit and reviewed available neuroimaging.

**Results:** Mean age was 11.88±6.53 years; period of gestation at birth: 33.26±4.78 weeks. 33/54 (61%) showed ONH pallor or cupping. Of 17 patients with ONH pallor, 88% were quadriplegic and 82% non-ambulatory. Mean cup/disc ratio was 0.45±0.22; 50% patients had large cup. Multivariate logistic regression models showed that disc cupping was significantly associated with non-ambulatory status (OR: 12.5; p=0.03) and quadriplegia (OR: 21.7; p=0.0025) and large cup was associated with age at examination (OR 1.15; p=0.025). Cup/disc ratio and age showed positive correlation (r=0.42; p=0.002). ONH parameters were not statistically associated with POG at birth.

**Conclusions:** ONH changes are common in POSE and are not associated with POG. Optic disc cupping, a bedside clinical finding is a prognostic indicator for severe neurological insult in high-risk children with perinatal complications that should prompt early referral for rehabilitation. Optic disc cupping is correlated with the age at examination which may indicate that the cupping worsens with age.

**Commercial Relationships:** Deepta Ghate, None; Veda Vedanarayanan, None; James Corbett, None; Abdulbaset Kamour, None; Sachin Kedar, None
Purpose: Temporal arteritis is an ophthalmic emergency and requires prompt treatment to prevent vision loss. The gold standard for diagnosis is the temporal artery biopsy. Current literature describes a positive biopsy as revealing chronic granulomatous inflammation at the level of the internal elastic lamina. The purpose of this study was to verify the location of most severe inflammation within a positive temporal artery and study other characteristics of our series in comparison to previous reports.

Methods: The list of patients with biopsy-proven temporal arteritis was generated by searching the University of Wisconsin Eye Pathology Laboratory database for the terms “giant cell arteritis” and “temporal arteritis.” Charts and pathology slides for patients from the last 15 years (1999 to present) were reviewed (n = 32). Cases with indeterminate diagnoses were excluded, as were cases where clinical information was unavailable.

Results: The average age of onset was 76.2 years, with 81% (26/32) of positive cases diagnosed in women. Patients were treated with oral steroids for an average of 4.25 days prior to biopsy. Unilateral temporal artery biopsies were submitted in 91% of cases (29/32); the remaining biopsies were bilateral. Both arteries were positive in two of the bilateral cases; one was positive and the other negative in the third case. The average artery sample length was 20 mm. Histopathologic features of the positive biopsies included intimal hyperplasia (32/32), lymphocytes (32/32), epithelioid cells (32/32), giant cells (29/32), fragmented internal elastic lamina (29/32), lumen narrowing (18/32), and concomitant Monckeberg’s arteriosclerosis (15/32). Skip areas were noted in 9% (3/32) of cases. The most severe inflammation was at the level of the media and adventitia in 37% of biopsies (12/32); the remaining had full thickness inflammation. No biopsies had inflammation isolated at or centered on the internal elastic lamina.

Conclusions: In contrast to the current literature, biopsies of patients with temporal arteritis reveal the principal focus of chronic granulomatous inflammation to be at the level of the media and adventitia or throughout the layers of the artery, not at the level of the internal elastic lamina. Other findings are generally consistent with previous reported series. Our findings lead us to hypothesize that the muscularis and adventitia may play an inciting role in the pathogenesis of temporal arteritis.

Commercial Relationships: Angeline Wang, None; Krishna Surapaneni, None; Daniel M. Albert, None
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Program Number: 5557 Poster Board Number: B0128
Presentation Time: 8:30 AM–10:15 AM
Final Diagnosis in Headache Patients Following Temporal Artery Biopsy
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Purpose: Giant cell arteritis (GCA) is a diagnosis made based on a combination of signs, symptoms and laboratory evidence (1). Temporal artery biopsy is the gold standard for the diagnosis of GCA and a referral for biopsy is commonly encountered entity in oculoplastic surgery practice (2). Our review investigates the final diagnosis and clinical course of headache patients undergoing temporal artery biopsy with the suspicion of giant cell arteritis (GCA). To our knowledge, this series of 143 patients is the largest study to date evaluating the final diagnosis in temporal artery biopsy patients from a single institution.

Methods: Retrospective chart review of 143 patients who underwent a temporal artery biopsy from January 2006 to April 2014 by vascular surgery, plastic surgery and oculoplastic surgery at our institution.

Results: Of 143 patients, 15 had positive biopsies (10.5%) and 128 had negative biopsies. Among the patients with negative biopsies, 41 patients (28.7%) ultimately were given the diagnosis of a benign headache. Biopsy-negative GCA was diagnosed when the American College of Rheumatology classification (7) criteria were met, symptoms improved within 3 days of corticosteroid therapy and no other diagnosis relevant to the patient’s presenting symptoms was diagnosed. 30 patients (20.9%) were ultimately diagnosed with biopsy-negative GCA. Of the remaining negative biopsies, 7 (4.9%) were found to have non-arteritic anterior ischemic optic neuropathy, 3 (2.1%) had isolated polymyalgia rheumatic, 3 (2.1%) with systemic vasculitis, 3 (2.1%) with acute angle closure, 3 (2.1%) with hypertensive urgency, 2 (1.4%) with posterior ischemic optic neuropathy, and 2 (1.4%) with granulomatosis with polyangiitis.

Conclusions: Even though only 15 patients (10.5%) had positive temporal artery biopsies, a total of 45 patients (31.5%) were ultimately treated for giant cell arteritis. Although the majority of patients (41 patients or 28.7%) undergoing temporal artery biopsy were diagnosed with benign headache, it is important to consider other vision and life threatening entities when presented with a patient with suspected GCA.

Program Number: 5558 Poster Board Number: B0129
Presentation Time: 8:30 AM–10:15 AM
Acute ischemic stroke in monocular vision loss of vascular etiology
Lucy Zhang1, Richard Kim1, Danielle Rudich1, Robert Lesser2 3, David Greer1, Hardik Amir1. 1Ophthalmology and Visual Sciences, Yale University, New Haven, CT; 2Neurology, Yale University, New Haven, CT; 3Yale University School of Medicine, New Haven, CT; 4The Eye Care Group, New Haven, CT.

Purpose: To evaluate the rate of co-occurrence of acute ischemic stroke and monocular vision loss of vascular etiology, as diagnosed by magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI). Two recent retrospective studies have shown that...
patients with monocular vision loss of ischemic origin are also more likely to have acute brain infarcts; however, these studies did not exclude patients with concurrent focal neurologic deficits (totaling 13-15% of their study populations). The goal of our study is to evaluate the likelihood of subclinical acute stroke identified on DWI in patients presenting with isolated monocular vision loss.

**Methods:** A retrospective analysis was performed using medical records from February 2013 through August 2014 at Yale-New Haven Hospital of patients who were diagnosed with monocular vision loss. Patients whose vision loss was likely related to a vascular etiology (such as amaurosis fugax or central or branch retinal vascular occlusion) and who underwent brain MRI within a seven day period were included. We determined the proportion of patients with monocular vision loss and acute stroke on brain MRI.

**Results:** A total of 448 records were reviewed. Of these, 293 patients had monocular vision loss of suspected or confirmed vascular etiology. Seventy-four patients were excluded due to the presence of other focal neurologic symptoms. Of the remaining 219 patients, 54 underwent MRI of the brain within seven days of the onset of symptoms, and 13 (24%) were found to have evidence of acute ischemic stroke based on restricted diffusion.

**Conclusions:** Patients with monocular vision loss due to amaurosis fugax, CRAO, or BRAO may have up to 24% risk of ischemic stroke as a result of thromboembolic phenomena. This study provides further evidence that ophthalmologists should refer monocular vision loss patients for neurologic evaluation and brain MRI with DWI even when vision loss is the isolated symptom.

**Commercial Relationships:** Lucy Zhang, None; Richard Kim, None; Daniiele Rudich, None; Robert Lesser, None; David Greer, None; Hardik Amin, None

**Program Number:** 5559 Poster Board Number: B0130

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

**Chiasmal syndrome: clinical features in Mexican patients, a 5 year review**

Aline Astorga-Carballo, Juan Carlos Serna-Ojeda, Mayra F Camargo. Instituto de Oftalmología Fundación Conde de Valencia I.A.P., Mexico City, Mexico.

**Purpose:** To evaluate the ocular manifestations of intracranial pathology producing a chiasmal syndrome, for those initially diagnosed or referred to an ophthalmologic institution.

**Methods:** An observational and retrospective study was performed with review of the records of all the patients with a diagnosis of chiasmal syndrome at an ophthalmologic reference center in a 5-year period. The variables analyzed included: demographic data, reason for consultation, visual acuity, visual field defect in Goldmann’s perimetry, afferent pupillary defect, changes in the color vision test, characteristics of the optic nerve and cranial imaging.

**Results:** 104 patients were included with a median age of 52 years (range 4 – 86 years). 54 patients (51.9%) were initially diagnosed because of the ophthalmologic examination, and 50 (48.07%) were referred with the presumptive diagnosis of an intracranial tumor. The median visual acuity at the time of diagnosis was 20/60 in the eye with worst vision, with 41 patients with a vision in one eye severely affected (worst than 20/400). The main symptoms were decreased central vision in 57 patients (54.8%) and changes in the peripheral visual field in 20 (19.2%); other aggregated manifestations like headache and systemic signs for elevated pituitary hormones were present in 10 (9.61%) and 18 cases (17.3%) respectively. Nine patients had a misdiagnosis of glaucoma for years. The most common visual field defect was bitemporal hemianopsia in 59 (56.73%), 54 patients (51.92%) had relative afferent pupillary defect, and in 65 (62.5%) the color vision test was affected. The optic nerve presented changes in 64.4% of the population. Cranial imaging confirmed the presence of an intracranial tumor in 23 cases (22.11%), being the most common pathology a pituitary adenoma.

**Conclusions:** Ophthalmologic examination could imply the initial diagnosis of intracranial pathology as the ocular manifestations are varied. Decreased vision is a common reason for consultation in patients with chiasmal syndrome, and other neurologic and systemic findings can be present. Complimentary study findings of intracranial pathology include bitemporal hemianopsia in Goldmann’s perimetry, altered color vision test and diagnostic cranial imaging.

**Commercial Relationships:** Aline Astorga-Carballo, None; Juan Carlos Serna-Ojeda, None; Mayra F. Camargo, None

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

**Proposing a new mechanism for chiasmal visual field loss in an unusual case of junctional scotoma: the degree of stretch of the anterior optic chiasm closely relates to the pattern of visual loss in a patient**

Yevgeniy Sychev, Raghu C. Mudumbai. University of Washington, Seattle, WA.

**Purpose:** To report a case of an unusual junctional scotoma in a patient produced via a stretching of an anterior aspect of the optic chiasm.

**Methods:** A single case report describing a patient with an unusual mechanism of junctional scotoma is presented.

**Results:** We present a case of an unusual junctional scotoma resulting from compression of the anterior optic chiasm by a pituitary macroadenoma. A patient presented complaining of unilateral vision loss in the left eye. Automated Humphrey visual field demonstrated dense temporal hemianopsia in the left eye and only trace visual field change in the left eye. Magnetic Resonance Imaging demonstrated a macroadenoma under the anterior aspect of the optic chiasm resulting in marked stretch of the chiasm in the horizontal coronal axis. Following surgical decompression the visual field deficit has resolved. (see figure) Postoperative imaging demonstrated marked reduction in the degree of chiasm stretch.

**Conclusions:** The visual field deficit observed in the presented case cannot be explained by the classic theory that states that dysfunction of visual axons stems from their compression at the chiasm. The deficit observed is neither a bitemporal hemianopsia, nor a typical junctional scotoma seen in syndromes of the middle and anterior chiasm compression respectively. Instead, the presented visual field defect implies involvement of predominantly the nasal fibers of the left optic nerve with sparing of the left temporal fibers and the right optic nerve. Pure compressive forces on the chiasm does not easily explain this pattern of visual loss. Close correlation between the degree of chiasm stretch and development of the temporal scotoma in this patient suggests that stretch of nerve fibers likely played an important role. The perpendicular relationship of the uncrossed fibers of the left optic nerve to the tumor with minimum lateral stretch forces at the chiasm may have lead to their relative protection. The crossing fibers may have been injured because of their partially parallel course to the horizontal stretch forces in the anterior chiasm from the tumor. This mechanism of optic neurologic dysfunction may also be important contributor in other cases of bitemporal and junctional scotomas.
MRI T1 sequence demonstrating compression of the optic chiasm.

Humphrey visual field obtained prior to optic chiasm decompression.

Humphrey visual field obtained two months after optic chiasm decompression.

Commercial Relationships: Yevgeniy Sychev, None; Raghu C. Mudumbai, None