Combined inhibition of angiotensin II type 1 receptor and ASK1 significantly attenuates autoimmune optic neuritis

Xiaoli Guo, Kazuhiko Namekata, Chikako Harada, Takayuki Harada. Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan.

**Purpose:** To study the effects of combined inhibition of angiotensin II type 1 receptor (AT1R) and apoptosis signal-regulating kinase 1 (ASK1), a mitogen-activated protein kinase kinase kinase (MAP3K), on optic neuritis in mice with experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis.

**Methods:** We induced EAE in female wild-type and ASK1-deficient mice. The effects of angiotensin II (AngII), the principal effector molecule of the renin-angiotensin system (RAS), and Toll-like receptor (TLR) signaling on EAE were examined. Clinical signs were scored daily and visual function was assessed by multifocal electroretinograms. Histopathological analysis of spinal cords and optic nerves was performed. Primary cultured astrocytes and bone marrow-derived dendritic cells (DC) were used to elucidate the relationship between AngII and TLR expression.

**Results:** We demonstrated that AngII expression is increased in the early phase of EAE and AngII induces TLR4 expression via an NF-κB pathway in astrocytes and DCs. Since we previously demonstrated that ASK1 binds to TLR4 and regulates innate immune responses, we examined possible interactions between the RAS and ASK1 signaling. Combined application of an AT1R antagonist, NF-κB nuclear translocation inhibitor and ASK1 inhibitor suppressed chemokine productions in astrocytes and DCs, reduced antigen-presentation capability of DCs and T cell proliferation. Consistent with these findings, in vivo administration of an AT1R antagonist to ASK1-deficient mice significantly reduced the incidence of EAE, and attenuated demyelination in spinal cords and optic nerves, retinal ganglion cell death and visual impairment.

**Conclusions:** Our findings suggest a novel pathway of RAS-NF-κB-TLR4-ASK1 in neural and immune cells as a valid therapeutic target for optic neuritis. Prescribed drugs to treat high blood pressure may be available for the prevention and treatment for neuroinflammatory diseases.

**Commercial Relationships:** Xiaoli Guo, None; Kazuhiko Namekata, None; Chikako Harada, None; Takayuki Harada, None

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**Program Number:** 5770 Poster Board Number: B0106

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

Dock8 and Dock10 regulate severity of inflammatory demyelination disorders


**Purpose:** Dock8, an atypical guanine nucleotide exchange factor (GEF) for Rho-family of small GTPases, has gained much attention since the discovery of Dock8 mutations in a combined immunodeficiency syndrome in humans. However, it is unknown whether Dock8 deficiency may be effective in inflammatory demyelinating disorders including optic neuritis. Therefore, we investigated roles of Dock8 andDock10, a homologue of Dock8, in inflammatory demyelination.

**Methods:** Three transgenic mouse lines were generated: Dock8 deficient (Dock8 KO); Dock8 overexpressing (Dock8 Tg); and Dock10 deficient (Dock10 KO) mice. We induced experimental autoimmune encephalomyelitis (EAE) by myelin oligodendrocyte glycoprotein (MOG) immunization in these transgenic mice. T-cell activations and proliferations were measured using FACS. Clinical signs were scored daily and visual function was assessed by multifocal electroretinograms. Histopathological analysis of optic nerves and spinal cords was performed.

**Results:** T-cell numbers in spleen were significantly reduced in Dock8 KO mice, but not in Dock8 Tg and Dock10 KO mice. Dock8 deficiency absolutely protected the optic nerve and spinal cord from inflammatory demyelination indicating that Dock8 is required to elicit autoimmune T-cell responses. The disease incidence was nearly halved in Dock8 Tg mice, and diseased EAE mice showed markedly decreased clinical signs, in which recovery was observed at later timepoints. In addition, a similar amelioration of inflammatory demyelination was observed in Dock10 KO mice; this resulted from suppression of cytokine production, namely, MIP-1α and MCP-1, in glial innate immunity.

**Conclusions:** Our findings suggest that manipulation of Dock8 and Dock10 signaling may serve as a novel therapeutic strategy against inflammatory demyelinating disorders.

**Commercial Relationships:** Kazuhiko Namekata, None; Xiaoli Guo, None; Atsuko Kimura, None; Chikako Harada, None; Takayuki Harada, None

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

HE3286 Reduces Axonal Loss and Preserves Retinal Ganglion Cell Function in Experimental Optic Neuritis

Reesa Sulaimankutty1, Kimberly Dine1, Esteban Luna1, Clarence Ahlem1, Kenneth S. Shindler1. 1Ophthalmology, Univ of Pennsylvania, Scheie Eye Inst, Philadelphia, PA; 2Harbor Therapeutics Inc, San Diego, CA.

**Purpose:** Optic nerve inflammation, demyelination and axonal loss are all prominent features of optic neuritis. While corticosteroids can hasten visual recovery in optic neuritis, no treatment is available to improve visual outcomes. HE3286 (17α-ethyl-5-androstene-3β, 7β, 17β-triol), a synthetic derivative of a natural steroid, β-AET (5-androstene-3β, 7β, 17β-triol), exerts anti-inflammatory effects in several disease models, and has purported direct neuroprotective effects as well. The ability of HE3286 to suppress optic neuritis in the experimental autoimmune encephalomyelitis (EAE) model of multiple sclerosis was examined.

**Methods:** HE3286 was administered in C57/B16 mice by immunization with myelin oligodendroglial glycoprotein peptide. Mice were treated daily with vehicle or 40 mg/kg HE3286 i.p. Visional function was assessed by optokinetic responses (OKR) at baseline and every 10 days until sacrifice 6 weeks post-immunization. Retinas and optic nerves were isolated. Inflammation was assessed by H&E staining, demyelination was assessed by luxol fast blue staining and axonal loss was assessed by neurofilament staining of optic nerve sections. Retinal ganglion cells (RGCs) were immunolabeled with Brn3a antibodies to quantify RGC survival.

**Results:** Progressive decreases in OKR occurred in vehicle-treated EAE mice, and HE3286 treatment significantly reduced the level of this vision loss. HE3286 also significantly attenuated the degree of...
inflammation, demyelination and axonal loss in EAE optic nerves as compared to nerves from vehicle-treated EAE mice. RGC loss was observed in eyes from both vehicle- and HE3286-treated EAE mice, with a trend toward increased RGC survival in the HE3286-treated mice.

Conclusions: HE3286 suppresses inflammation and reduces demyelination and axonal loss during experimental optic neuritis. Importantly, HE3286 treatment also preserves some RGC function. Results suggest HE3286 is a potential novel treatment for optic neuritis and MS that warrants further study.

Commercial Relationships: Reas Sulaimankutty, None; Kimberly Dine, None; Esteban Luna, None; Clarence Ahlem, Harbor Therapeutics (E), Harbor Therapeutics (I); Kenneth S. Shindler, Harbor Therapeutics (F)

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Program Number: 5772 Poster Board Number: B0108
Presentation Time: 8:30 AM–10:15 AM

Resveratrol and BBI combination therapy in experimental optic neuritis

Purpose: Optic neuritis, an inflammatory demyelinating optic nerve disease in multiple sclerosis, is modeled in mice with experimental autoimmune encephalomyelitis (EAE). Resveratrol (RSV), a naturally-occurring polyphenol that activates the SIRT1 deacetylase, can prevent retinal ganglion cell (RGC) loss without suppressing inflammation in chronic EAE. Bowman-Birk Inhibitor (BBI) is a naturally-occurring protease inhibitor that prevents RGC loss by suppressing inflammation in relapsing EAE. This study used combination therapy of RSV+BBI in chronic EAE optic neuritis to measure synergistic effects.

Methods: EAE was induced in C57/B16 mice by immunization with myelin oligodendroglial glycoprotein peptide. Wild type immunized mice were left untreated, or treated daily with 250 mg/kg RSV, 1 mg BBI, or both RSV+BBI. Negative control mice were sham immunized with PBS. Mice were observed and scored daily for clinical signs of EAE (ascending paralysis). Visual function was assessed by optokinetic responses (OKR) at baseline and each week until sacrifice 6 weeks post-immunization. Retinas and optic nerves were isolated. Inflammation was assessed by H&E staining, demyelination was assessed by luxol fast blue staining, and axonal loss was assessed by neurofilament staining of optic nerve sections. RGCs were immunolabeled with Brn3a antibodies to quantify RGC survival.

Results: RGC function, assessed by OKR, decreased in untreated EAE mice. The decrease in OKR was significantly reduced by treatment with RSV, BBI and RSV+BBI. There was an increase in the degree of inflammation in optic nerves of untreated EAE mice compared to non-EAE control mice. RSV and BBI treatment alone each showed a trend toward decreased optic nerve inflammation, but inflammation was significantly attenuated only by combined treatment with RSV+BBI. There was no significant RGC loss, axonal loss, or demyelination in untreated EAE mice or treated mice. BBI and RSV+BBI treatment decreased clinical signs of EAE.

Conclusions: RSV+BBI helped preserve vision, decreased inflammation severity, and decreased clinical signs of EAE. This combination therapy was more effective than treatment with either compound alone. Results suggest that combined RSV+BBI is a potential therapeutic approach for limiting vision loss from optic neuritis.

Commercial Relationships: Esteban Luna, None; Reas Sulaimankutty, None; Kimberly Dine, None; Kenneth S. Shindler, None
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Program Number: 5773 Poster Board Number: B0109
Presentation Time: 8:30 AM–10:15 AM

Distribution of OPA1-AS1 genetic variants in patients with optic atrophy

Purpose: Mutations in OPA1 on chromosome 3q28 account for between 30 and 60% of dominant optic atrophy (DOA) cases. Although OPA1 mutation carriers frequently exhibit inter- and intra-familial phenotypic variability, factors impacting OPA1 variable expressivity are not yet known. OPA1 antisense RNA 1 (OPA1-AS1) is a long non-coding miRNA that extends from introns 5 to intron 7 of the OPA1 gene. OPA1-AS1 may function to regulate the expression of OPA1. This study aims to identify OPA1-AS1 genetic variants in optic atrophy patients and to investigate the impact of these variants on the clinical phenotype.

Methods: The study was approved by the Massachusetts Eye and Ear Infirmary Institutional Review Board. Fifty-four optic atrophy patients and 216 controls were studied. Genomic DNA was extracted from each subject and sequenced using primers designed to amplify all 3 exons in OPA1-AS1. The 10-20 basemaps of the flanking introns were also included in the targeted sequence. PLINK was used for estimation of haplotype frequencies and for haplotype association analysis. Multiple testing corrections were performed with 10,000 permutation tests. Linear regression was used to interrogate the association of OPA1-AS1 variants with continuous data under the assumption of an additive genetic effect.

Results: OPA1-AS1 sequencing identified four variants: rs9832709, rs3772393, and rs34307082 in exon 3 and rs9291059 in intron 1. Novel variants in OPA1-AS1 were not found. We found that an OPA1-AS1 haplotype was more common in optic atrophy cases (50.6%) than in controls (34.6%) (Corrected P = 0.0054). This haplotype frequency was similar in both cases with OPA1 mutations (58.3%) and in cases without OPA1 mutations (50.7%). There was an additive genetic effect of rs9832709 on age of disease diagnosis, suggesting that carriers of the C allele have an earlier age of onset (7.2 ± 4.5 years per allele). However, this was not statistically significant in the overall linear regression analysis (P = 0.113). Other phenotypic features, including visual acuity and visual field parameters, were not different among the genotype groups.

Conclusions: DOA patients have a different distribution of the variants in OPA1-AS1 compared to normal controls. While not statistically significant in this patient cohort, variants in OPA1-AS1 may influence the age of onset of optic atrophy. Further study will be required to confirm this finding.

Commercial Relationships: Isao Nakata, None; Eric D. Gaier, None; Maria Janessian, None; Elizabeth Delbono, None; Louis R. Pasquale, None; Simmons Lessell, None; Dean M. Cestari, None; Joseph F. Rizzo, None; Janey L. Wiggs, None
Support: Bausch & Lomb Japan
Optical Coherence Tomography in Multiple Sclerosis Patients

Lucy T. Xu, Robert A. Bermel, Amy Nowacki, Peter K. Kaiser.
1Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, OH; 2Mellen Center for Multiple Sclerosis, Cleveland Clinic, Cleveland, OH; 3Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH; 4Cole Eye Institute, Cleveland Clinic, Cleveland, OH.

Purpose: Do multiple sclerosis (MS) patients with optic neuritis exhibit differences in OCT, functional, and/or visual acuity measures compared to MS patients without optic neuritis and healthy controls?

Methods: Prospective case-control study of 30 MS-optic neuritis patients, 22 MS-non optic neuritis patients and 24 healthy controls. Full contrast visual acuity (FCVA), 2.5% and 1.25% Sloan low contrast visual acuity (LCVA), Visual Functioning Questionnaire-25 (VFQ-25), Multiple Sclerosis Performance Scale (MSPS) scores, and Cirrus HD-OCT and Spectralis HRA+OCT scans in both the peripapillary and macular regions were obtained.

Results: Optic neuritis eyes exhibited thinner average peripapillary retinal nerve fiber layer (RNFL), papillomacular bundle (PMB), ganglion cell + inner plexiform layer (IPL), macular RNFL and average macular thickness compared to MS eyes without optic neuritis and healthy controls. The macular volumes of optic neuritis eyes were also significantly less. Total macular volume, central subfield thickness, and nasal and temporal RNFL measurements were statistically different (p < 0.03) between Cirrus and Spectralis while average peripapillary RNFL thickness did not differ significantly (p = 0.24). We show that PMB and ganglion cell + IPL are equally and significantly correlated with 2.5% LCVA (r = 0.54). Ganglion cell + IPL thickness seems to correlate more highly than PMB with 1.25% LCVA. However, in subjective measures of visual function (VFQ-25 and MSPS vision subscore), PMB correlates more highly than ganglion cell + IPL. We found PMB thickness to be the best predictor in discriminating between optic neuritis and non-optic neuritis eyes in MS patients while visual acuities were rather poor predictors.

Conclusions: The structural differences seen in optic neuritis eyes correlate well with functional changes in visual acuity, and quality of life as it relates to vision. Also, there exist discrepancies in various OCT measurements across machine types due to scan patterns and/or segmentation algorithms. In MS patients, optic neuritis eyes can be differentiated from non-optic neuritis eyes using PMB thickness. This work exhibits the unique and important role of OCT in understanding differentiaed from non-optic neuritis eyes using PMB thickness. Further studies will continue to work exhibits the unique and important role of OCT in understanding differentiaed from non-optic neuritis eyes using PMB thickness. This work exhibits the unique and important role of OCT in understanding different
ON. In MSEs the thickness of PGCL does not correlate with FS; it is possible that in MSEs most of the GC lost were not involved in the FS response.

Commercial Relationships: Andrea M. Coppe, None; Giuliana Lapucci, None; Guido Ripandelli, None

Program Number: 5777 Poster Board Number: B0113
Presentation Time: 8:30 AM–10:15 AM
Relation between retinal ganglion cell-inner plexiform layer thickness (GCIPT) and multifocal visual evoked potentials (mfVEP) in relapsing-remitting multiple sclerosis (RRMS) patients
Divya Narayanan1, Han Cheng1, Rosa Tang2, Laura Frishman1.
1College of Optometry, University of Houston, Houston, TX; 2MS Eye Care clinic, University of Houston, Houston, TX.
Purpose: To examine the relation between GCIPT, measured by optical coherence tomography (OCT) and visual function, in RRMS eyes.
Methods: Cirrus OCT, mfVEP and Pelli-Robson contrast sensitivity (CS) were obtained from 90 RRMS patients. One eye from each was randomly selected for analysis (37 eyes with last optic neuritis (ON) ≥6 months and 53 no-ON eyes). mfVEP, recorded with 60-sector cortically-scaled dartboard pattern-reversal stimulus (22° radius, VERIS 5.1), provided local response amplitude (logSNR) and latency (ms). Global and central 5.6° mfVEP amplitude and latency were calculated as mean logSNR (or median SNR) and median latency from all 60 and central 24 sectors, respectively.[1] 76 eyes had Humphrey visual field (HVF) 24-2 or 30-2; 23 eyes had HVF 10-2. Relative visual sensitivity (RVS) was calculated as average unlogged local deviation. Traditional pattern-reversal VEP (tVEP) was recorded in 30 patients (22° radius stimulus); p100 amplitude and latency measured. Pearson correlation was assessed between structural measures, GCIPT and average retinal nerve fiber layer thickness (RNFLT), and functional measures.
Results: Both ON and no-ON eyes showed significant structure-function correlations, ON higher. For all eyes, among functional measures, GCIPT showed the highest correlation with mfVEP central 5.6° logSNR (r=0.72 p<0.0001; r=0.63 for SNR, p<0.0001) followed by CS (r=0.63, p<0.0001). GCIPT showed moderate correlation with 10-2 RVS (r=0.49, p<0.03) but no correlation with tVEP amplitude. RNFLT showed moderate to good correlation with mfVEP global logSNR (r=0.55, p<0.0001), CS (r=0.63, p<0.0001), weak correlation with 24-2/30-2 RVS (r=0.23, p=0.05) and no correlation with tVEP amplitude. GCIPT also showed good correlation with mfVEP central 5.6° latency (r=0.48, p=0.0001) and tVEP latency (r=0.69, 0.48 for 15°, 60°, 120° checks, p<0.0001).
Conclusions: GCIPT correlated well with mfVEP amplitude and latency. GCIPT and mfVEP provide useful structural and functional measures of macular ganglion cells in RRMS.
Commercial Relationships: Divya Narayanan, None; Han Cheng, None; Rosa Tang, None; Laura Frishman, None
Support: NIH P30 EY07551, NIH T35 007088, Fight for Sight summer student fellowship and the Minnie Flaura Turner memorial fund for impaired vision research

Program Number: 5778 Poster Board Number: B0114
Presentation Time: 8:30 AM–10:15 AM
Evaluation of Retinal Nerve Fiber Layer in patients with idiopathic Optic Perineuritis using Optical Coherence Tomography
Jae Ho Jung1, Jong Heon Lee1, Kyong Ho Kim1, Ik Soo Byon1, Je Hyun Seo2, Ji Eun E. Lee, Hee-Young Choi1.
Purpose: Optic perineuritis (OPN) is an uncommon inflammatory disorder of the optic nerve sheath. It has been reported that the diagnosis of OPN may be poor when initiation of treatment is delayed. The aim of this study is to assess the effect of optic nerve sheath inflammation on retinal nerve fiber layer (RNFL), and the ability of optical coherence tomography(Oct) to evaluate the retinal nerve fiber loss after idiopathic optic perineuritis (OPN)
Methods: The diagnosis of OPN was made in patients who had an acute optic neuropathy and radiographic demonstration of enhancement of the optic nerve sheath in fat suppression and contrast enhancement orbital magnetic resonance imaging (MRI).
All patients underwent laboratory testing to exclude specific systemic inflammatory diseases: the complete blood cell count, the erythrocyte sedimentation rate, and the levels of antinuclear antibodies and angiotensin-converting enzyme were determined; a syphilis serologic test was performed; and a chest x-ray film was obtained. We excluded patients who were diagnosed intraocular disease, systemic disorder associated with orbital inflammation, systemic infectious disease and neoplastic condition. We analyzed 4 OPN patients; symptoms, visual acuity, color vision, automated visual field, optic disc appearance, and OCT. Subjects were underwent by Cirrus Spectral Domain-OCT (Carl Zeiss Meditec, Inc.,Dublin, CA) and the OCT parameters, optic nerve head and RNFL thickness, was calculated automatically by the equipment’s software at initial visit and 12 months follow-up.
Results: All patient showed decreased visual acuity, abnormal color vision, visual field defect. Average and temporal sector RNFL thickness of affected eye was 86.75 um, 85.25 um at initial visit and was 76.75 um, 53 um after 12months, which means especially temporal sector RNFL (Papillomacular bundle) was significant thinner in affected eye when compared to normal value and the other sound eye at 12 months after acute OPN.
Conclusions: Our study suggests that retinal nerve fiber loss was observed in idiopathic optic nerve sheath inflammation and OCT was good technique for axonal loss and disease severity indicator in OPN
Commercial Relationships: Jae Ho Jung, None; Jong Heon Lee, None; Kyong Ho Kim, None; Ik Soo Byon, None; Je Hyun Seo, None; Ji Eun E. Lee, None; Hee-Young Choi, None

Program Number: 5779 Poster Board Number: B0115
Presentation Time: 8:30 AM–10:15 AM
Measurements by Spectral Domain OCT in Papilledema are Associated with Reduced Retinal Nerve Fiber Layer Thickness after Resolution of Optic Disc Swelling
Berthold Pump, Andreas Rettern, Karl Kircher, Ursula Schmidt-Erfurth. Department of Ophthalmology, Medical University of Vienna, Vienna, Austria.
Purpose: Papilledema induced by increased intracranial pressure can result in considerable axonal damage and permanent loss of optic nerve fibers. It is, however, difficult to determine the degree of atrophic changes in swollen optic discs. Hence this study was performed to test whether individual features of optic disc morphology and peripapillary retinal nerve fiber layer (RNFL) thickness distribution in optical coherence tomography (OCT) of

active papilledema are associated with nerve fiber atrophy after resolution of the swelling.

**Methods:** 40 patients with papilledema due to primary pseudotumor cerebri were included in this study. Measurements of peripapillary RNFL thickness using spectral OCT at the time of presentation and after resolution of papilledema were analyzed. Radial cross sections were used to measure intrabulbar elevation of the optic nerve head above Bruch’s membrane. Patients with sectoral atrophy of the RNFL after complete resolution of papilledema were compared to patients without atrophy using unpaired t-tests. In addition, Pearson product-moment correlation coefficients were calculated to assess correlations between measured parameters.

**Results:** 23% of the analyzed eyes showed marked sectoral atrophy of the RNFL. The initial maximum elevation of the swollen optic nerve head was found significantly higher in patients with subsequent sectoral atrophy (1155 ± 235 μm vs. 1023 ± 156 μm, p = 0.036). In addition, peripapillary RNFL thickness after resolution of papilledema correlated negatively with initial optic nerve head elevation (r = -0.51, p < 0.001) but not with initial RNFL thickness (r = -0.11, p = 0.334). Sectoral comparison of initial maximum and minimum RNFL thickness showed a significantly higher difference in eyes with subsequent sectoral atrophy (200 ± 61 μm vs. 166 ± 54 μm, p = 0.036).

**Conclusions:** Our results indicate that the extent of optic nerve head elevation in papilledema caused by increased intracranial pressure is associated with sectoral atrophy of retinal nerve fibers after resolution of the swelling. In addition, sectoral comparison of peripapillary RNFL thickness in present disease seems to indicate already damaged portions of the swollen nerve fiber layer.

**Commercial Relationships:** Berthold Pemp, None; Andreas Reitner, None; Karl Kircher, None; Ursula Schmidt-Erfurth, None

**Program Number:** 5780 **Poster Board Number:** B0116

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

**Retinal Ganglion Cell Layer Thinning and Vision Outcome in NAION and Optic Neuritis over Six Months**

Jui-Kai Wang1, Mark J. Kupersmith2, Mona K. Garvin1, Randy H. Kardon3, 4. 1Department of Electrical and Computer Engineering, The University of Iowa, Iowa City, IA; 2Department of Neuro-Ophthalmology, Roosevelt Hospital and NYEE, New York, NY; 3VA Center for the Prevention and Treatment of Visual Loss, Iowa City VA Health Care System, Iowa City, IA; 4Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA.

**Purpose:** We previously showed that retina ganglion cell layer (GCL) thinning occurs within one month of acute optic neuritis (ON) and non-arteritic anterior ischemic optic neuropathy (NAION), long before retinal nerve fiber layer (RNFL) thinning or complete loss of acute swelling are seen (ARVO 2013). Here we investigate the trajectory of GCL thinning over 6 months in both disorders in order to determine when most of the loss occurs and how the amount of GCL loss relates to the visual outcome.

**Methods:** Using spectral domain optical coherence tomography (SD-OCT, Cirrus 4000) of the optic nerve head and macula areas, we prospectively evaluated 29 eyes (age 36±10) with new onset ON and 29 eyes (age 65±12) with NAION within 2 weeks of vision loss (acute stage), at one month and at 6 months. We used 3D-segmentation to calculate the GCL plus inner plexiform layer thickness for each macula image.

**Results:** The maximum amount of GCL thinning occurred at 1 month with mean loss of 19.62 μm ± 12.62 for NAION and 8.68 μm ± 5.09 for ON eyes. A modest, further thinning of the GCL occurred between 3 and 6 months in NAION (6.11 μm and 1.11 μm, respectively) and in ON (2.61 μm and 0.62 μm, respectively). The amount of GCL thinning at 1 month strongly correlated with the amount of GCL loss at 6 months in NAION (r=0.854) and in ON (r=0.838) eyes. There was also a significant correlation between the GCL thickness at one month and the mean deviation of the visual field for NAION eyes (r=0.507) but not in ON eyes (r=0.052). The RNFL was thickened, particularly in NAION eyes, at presentation and 1 month and did not correlate with mean deviation of the visual field in either NAION or ON at that time point. The RNFL did not show thinning until the 3 and 6-month time points.

**Conclusions:** For acute ON and NAION, the largest proportion of GCL loss has already occurred at one month (in contrast to the RNFL, due to continued swelling) and suggests that neural preservation or protection therapy must be delivered earlier than one month to significantly prevent loss of retinal ganglion cells in both disorders.
Antioxidant Status of Uric Acid, Bilirubin and Albumin in Patients with Optic Neuritis

Juan Deng. Ophthalmology, The Third Affiliated Hospital of Sun Yat-sen University, GuangZhou, China.

Purpose: Uric acid UA, bilirubin and albumin are endogenous antioxidants. Previous studies have reported that their concentrations were reduced in patients with multiple Sclerosis (MS) and neuromyelitis optica NMO. The pathophysiology of optic neuritis ON resembles that of MS; however, the role of endogenous UA, bilirubin and albumin in ON are still unclear. The aim of this study is to analyze antioxidant levels of serum UA, bilirubin and albumin in patients with ON, and compare the antioxidant levels of ON with MS and NMO.

Methods: Serum levels of UA, bilirubin and albumin were measured in 42 patients with ON, 50 patients with MS, 48 patients with NMO and 48 healthy control subjects.

Results: Serum levels of UA, bilirubin and albumin in patients with ON were significantly lower than those in healthy control group. No statistical significance was found among ON, MS and NMO groups. The same results were still observed when the effect of gender was eliminated. Moreover, serum levels of UA, bilirubin and albumin in patients with ON were lower in those with recurrence or longer duration (≥1 year). Their concentrations were lower in patients with papillitis than in those with retrobulbar type ON, but the differences were not statistically significant.

Conclusions: Reduced serum UA, bilirubin and albumin levels are found in patients with ON, and low antioxidant status may exist in those patients. Since ON is often the first clinical demyelinating event of MS or NMO, our results may indicate that low antioxidant status already existed in MS or NMO.

Commercial Relationships: Juan Deng, None
Support: 2008B060600061

Program Number: 5781 Poster Board Number: B0117
Presentation Time: 8:30 AM–10:15 AM
Visual function and retinal nerve fiber layer thickness in Neuromyelitis optica: a longitudinal and comparative study

Rabih HAGE1, 2, Philippe Cabre1, Harold Merle1. 1Ophthalmology, Fort-de-France University Hospital, Fort-de-France, Martinique; 2Neuro-Ophthalmology, EMORY University, Atlanta, GA.

Purpose: Longitudinal studies in multiple sclerosis (MS) show that visual function decreases as a function of time and is correlated with a thickening of the retinal nerve fiber layer (RNFL) measured by optical coherence tomography (OCT). We determined the outcome of visual acuity and RNFL thickness in Neuromyelitis optica (NMO) in the lack of clinical relapse.

Methods: Patients underwent high and low-contrast visual acuity (2.5%, 1.25%), frequency doubling technology perimetry (FDTP) and OCT measurement of RNFL thickness at baseline and at least a year later.

Results: Among 42 patients with ≥1 year follow-up, 15 (30 eyes) were diagnosed with NMO and 27 (53 eyes) with MS. While every assessment in NMO eyes did not show any decrease, MS eyes without history of optic neuritis (ON) showed a worsening of 1.25% low contrast visual acuity (-4.81; p=0.04) and FDTP median deviation (-1.85; p=0.039). Furthermore, the whole MS eyes exhibited a significant loss of RNFL thickness (-4.56 μm; p<0.0001).

Conclusions: While visual function in NMO patient remain stable, progressive RNFL thinning occurs as a function of time in patients with MS, even in the absence of ON, and is associated with clinically significant visual loss. These findings are consistent with sub-clinical axonal loss in MS and the absence of chronic inflammation in NMO. Consequently, NMO therapeutic strategies would have been limited to the acute relapses treatment and prevention. Neuroprotection would not have any effectiveness in this disease.

Commercial Relationships: Rabih HAGE, None; Philippe Cabre, None; Harold Merle, None

Visual function and retinal nerve fiber layer thickness in Neuromyelitis optica: a longitudinal and comparative study

Rabih HAGE1, 2, Philippe Cabre1, Harold Merle1. 1Ophthalmology, Fort-de-France University Hospital, Fort-de-France, Martinique; 2Neuro-Ophthalmology, EMORY University, Atlanta, GA.

Purpose: Longitudinal studies in multiple sclerosis (MS) show that visual function decreases as a function of time and is correlated with a thickening of the retinal nerve fiber layer (RNFL) measured by optical coherence tomography (OCT). We determined the outcome of visual acuity and RNFL thickness in Neuromyelitis optica (NMO) in the lack of clinical relapse.

Methods: Patients underwent high and low-contrast visual acuity (2.5%, 1.25%), frequency doubling technology perimetry (FDTP) and OCT measurement of RNFL thickness at baseline and at least a year later.

Results: Among 42 patients with ≥1 year follow-up, 15 (30 eyes) were diagnosed with NMO and 27 (53 eyes) with MS. While every assessment in NMO eyes did not show any decrease, MS eyes without history of optic neuritis (ON) showed a worsening of 1.25% low contrast visual acuity (-4.81; p=0.04) and FDTP median deviation (-1.85; p=0.039). Furthermore, the whole MS eyes exhibited a significant loss of RNFL thickness (-4.56 μm; p<0.0001).

Conclusions: While visual function in NMO patient remain stable, progressive RNFL thinning occurs as a function of time in patients with MS, even in the absence of ON, and is associated with clinically significant visual loss. These findings are consistent with sub-clinical axonal loss in MS and the absence of chronic inflammation in NMO. Consequently, NMO therapeutic strategies would have been limited to the acute relapses treatment and prevention. Neuroprotection would not have any effectiveness in this disease.

Commercial Relationships: Rabih HAGE, None; Philippe Cabre, None; Harold Merle, None

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