7:30 a.m. - 7:45 a.m.  Bradley J. Katz, MD, PhD
A Phase I Open Label, Dose Escalation Trial Of QPI-1007 Delivered By A Single Intravitreal (IVT) Injection To Subjects With Low Visual Acuity And Acute Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)

7:45 a.m. - 8:00 a.m.  Victoria S. Pelak, MD
3D Radial Optic Flow Perception in Alzheimer’s Disease and Parkinson’s Disease with Advanced Motor Symptoms

8:00 a.m. - 8:15 a.m.  Sung Eun Kyung, MD, PhD
Enlargement of the Sella Turcica Partially Explains the Partially Empty Sella of Pseudotumor Cerebri

8:15 a.m. - 8:30 a.m.  Mark J. Kupersmith, MD
Acute Changes in Retinal Birefringence at Onset of NAION Reveals Axonal Injury Corresponding to Permanent Regional Visual Field Loss

8:30 a.m. - 8:45 a.m.  Kimberly M. Winges, MD
The Ganglion Cell Layer Across the Vertical Meridian in Hemianopsia: I Get No Respect!

8:45 a.m. - 9:00 a.m.  Kenneth S. Shindler, MD, PhD
SIR T1 Reduces Oxidative Stress and Delays RGC Loss Following Optic Nerve Crush

9:00 a.m. - 9:15 a.m.  Christian J. Lueck, PhD, FRACP, FRCP(UK)
Finite Element Modeling of Chiasmal Compression: Nearer to an Understanding of Bitemporal Hemianopia?

9:15 a.m. - 9:30 a.m.  Update: The Journal of Neuro-Ophthalmology
Lanning Kline, MD, Editor-in-Chief and Jason Roberts, PhD, Managing Editor

9:30 a.m. - 10:00 a.m.  Coffee Break: Ballroom 1
10:00 a.m. - 10:15 a.m.  Robert A. Avery, DO
Hand-Held Optical Coherence Tomography During Sedation Detects Visual Acuity and Visual Field Loss in Young Children with Optic Pathway Gliomas

10:15 a.m. - 10:30 a.m.  Kristina Irsch, PhD
Fusion Influences the Bielschowsky Head Tilt Test in Superior Oblique Paresis

10:30 a.m. - 10:45 a.m.  Cynthia Yu-Wai-Man, MBBS, FRCOphth
Extraocular Muscle Atrophy and Central Nervous System Involvement in Chronic Progressive External Ophthalmoplegia – A Structural and Spectroscopic Magnetic Resonance Study

10:45 a.m. - 11:00 a.m.  Randy Kardon, MD, PhD
The Light Induced Electromyogram Shows Exaggerated Responses in Patients with Photo-sensitivity

11:00 a.m. - 11:15 a.m.  Byron L. Lam, MD
Leber Hereditary Optic Neuropathy G11778A Gene Therapy Clinical Trial: Stability of Clinical Parameters in Preparatory Phase Based on Onset of Visual Loss

11:15 a.m. - 11:30 a.m.  Gregory P. Van Stavern, MD
Functional Connectivity in Patients With Clinically Isolated optic Neuritis

11:30 a.m. - 11:45 a.m.  Stacy Pineles, MD
Functional Burden of Strabismus: Decreased Binocular Summation (BiS) and Binocular Inhibition

11:45 a.m. - 12:00 p.m.  Jason H. Peragallo, MD
Surgical Outcomes in Adult Sixth Nerve Palsy
A Phase I Open Label, Dose Escalation Trial Of QPI-1007 Delivered By A Single Intravitreal (IVT) Injection To Subjects With Low Visual Acuity And Acute Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)

Bradley J. Katz1, A. Antoszyk2, R.P. Singh3, R. Gurses-Ozden4, S. Erlich4, D. Rothenstein4, N. Sharon4, J. Hodge4, L.A. Levin5,6, N.R. Miller7, QPI-1007 NAION Study Group8

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Introduction:
Subjects with stable low vision due to posterior segment pathology and subjects with acute onset NAION were enrolled in a 2 strata, Phase I, multi-center, open-label, and dose escalation study to determine safety, tolerability, and the structural and functional changes after single IVT injection of QPI-1007, a synthetic, chemically modified siRNA that inhibits expression of caspase 2.

Methods:
Low vision subjects with visual acuity (VA) ≤20/200 in 6 cohorts (0.2-6 mg) and NAION subjects with ≤20/40 and symptom onset within 28 days were dosed in 3 cohorts (1.2, 2.4 and 6.0 mg). After receiving a single IVT injection, subjects were evaluated for VA, visual field (VF) and retinal nerve fiber layer (RNFL) thickness at days 1, 7, 14, 28, and months 2, 3, 6, 12.

Results:
48 subjects (18 low vision, 30 NAION) were enrolled. Available data from all cohorts through Month 3 (n=48), Month 6 (n=43) and Month 12 (n=35) were analyzed. 256 of 268 adverse events (AEs) were of mild to moderate severity. There were no serious AEs. Among 28 NAION subjects with on-chart VA, maximum VA gain was at Month 2 (mean± SD: 16.4 ±10.4 letters). The proportion of subjects improving by ≥3 lines at Month 3 was 50.0%, compared with 39.7% of IONDT historical controls (p = 0.4, Fisher exact test). Similar improvement compared with historical controls was seen at months 6 and 12. No subject lost ≥3 lines at months 3 and 6 compared with 9.1% and 14.8%; respectively, in the historical controls.1 VF mean defect was comparable to baseline. RNFL loss was similar to historical controls.2

Conclusions:
A single IVT injection of QPI-1007 was well tolerated in subjects with stable low vision or recent-onset NAION. Further studies are needed to determine QPI-1007’s effect on visual function and RNFL thickness.

References:

Keywords: Ischemic Optic Neuropathy, Intravitreal Injection, Caspase 2, siRNA, QPI-1007

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3D Radial Optic Flow Perception in Alzheimer’s Disease and Parkinson’s Disease With Advanced Motor Symptoms

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Introduction:
Optic flow (the pattern of motion at the eye) controls human walking, and the disruption of visually-driven, cognitive neuronal networks involved in radial optic flow (ROF) processing contributes to spatial navigation errors in Alzheimer’s disease (AD).¹ These data are based on ROF motion stimuli presented in 2D, while 3D ROF stimuli (simulating real-life) have not been investigated in AD and may have different cognitive correlates. The specificity of impaired ROF perception is unknown since it has not been studied in other neurodegenerative diseases. The aim of this study was to compare the perception of 3D ROF patterns in healthy older adults (HOA), AD, and Parkinson’s disease subjects with advanced motor symptoms (PD-AMS).

Methods:
HOA (n=25), early AD (n=12), and PD-AMS (n=14) subjects without dementia or mild cognitive impairment (MCI), who were about to undergo deep brain stimulation (DBS), viewed expanding ROF patterns in a 3D, immersive, virtual environment. Discrimination thresholds for the focus of expansion were determined using standard parameter estimation techniques (ML-PEST). Threshold testing of PD-AMS subjects was repeated 4 to 6 months after DBS surgery.

Results:
Sensory thresholds revealed a significant group effect (F=32.7, p<0.001). In post hoc analysis, healthy and PD subjects were indistinguishable, while early AD subjects had significantly impaired perception of ROF patterns compared to healthy and PD subjects (p<0.001). There were no significant differences in pre- and post-DBS thresholds in PD-AMS subjects (p=0.53).

Conclusions:
Perception of 3D ROF patterns is disrupted in early AD (to a greater degree than reported with 2D stimuli), but not in patients with advanced motor symptoms due to PD without dementia or MCI. DBS did not alter ROF perception. Study of PD subjects with MCI, and with early dementia, is warranted to further assess whether impaired ROF perception is an important visuospatial biomarker specific to early AD.

References:

Keywords: Alzheimer's disease, Parkinson's disease, Optic Flow Motion Perception, 3D, Virtual Reality

Financial Disclosures: The authors had no disclosures.
Enlargement of the Sella Turcica Partially Explains the Partially Empty Sella of Pseudotumor Cerebri

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Introduction:
Neuroimaging frequently reveals a partially empty sella in patients with pseudotumor cerebri (PTC)1-3. It is thought to occur from compression of the pituitary gland by herniation of the subarachnoid space into the sella turcica4. We compared the size of the sella turcica in patients with PTC and normal control subjects to determine if enlargement of the pituitary fossa also contributes to the appearance of a partially empty sella.

Methods:
Imaging software (OsiriX) was used to measure the size of the sella turcica and pituitary gland in 48 females with (PTC) and 48 age-matched controls in a masked fashion. All patients met revised diagnostic criteria for PTC5. Papilledema was present in 45/48 subjects at the time of MR imaging; 3 had optic atrophy. The mean subarachnoid opening pressure was 336 ± 83 mm H2O.

Results:
In control subjects, the median sellar area was 63 mm2 (interquartile distance 26 mm2) and the mean sella area was 64 ± 17 mm2. In patients with PTC, the median sellar area was 87 mm2 (interquartile distance 38 mm2) and the mean sella area was 90 ± 30 mm2. The mean sellar area was 41% greater in PTC. The 95% confidence interval (82 mm2, 99 mm2) for patients with PTC did not overlap the 95% confidence interval (59 mm2, 69 mm2) for control subjects. There was a strong correlation between the area of the sella turcica and the percentage of the sella that was empty (Pearson’s correlation coefficient, r = 0.67, p < 0.001).

Conclusions:
Chronic intracranial hypertension in PTC leads to bony enlargement of the sella turcica. Compression of the pituitary gland against the floor of the sella causes it to expand, giving rise to a partially empty sella. The larger the sella, the more empty it appears.

References:

Keywords: Papilledema, Pituitary gland, Idiopathic intracranial hypertension, Cerebrospinal fluid, Sella turcica

Financial Disclosures: The authors had no disclosures.
Tuesday, February 12, 8:15 - 8:30 a.m.

Acute Changes in Retinal Birefringence at Onset of NAION Reveals Axonal Injury Corresponding to Permanent Regional Visual Field Loss

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Introduction:
Scanning laser polarimetry (SLP) can reveal acute injury (loss of birefringence) in non-arteritic anterior ischemic optic neuropathy (NAION) but not with other causes of optic nerve head swelling (IOVS 2012). We hypothesize that regional RNFL alterations, shown by SLP, in acute NAION can correlate with acute and chronic regional visual field deficits, providing an in vivo biomarker for irreversible injury of optic nerve axons.

Methods:
We prospectively evaluated 25 new NAION eyes with threshold perimetry, SLP and HD-OCT. We compared SLP and OCT average RNFL values, derived from Garway-Heath RNFL mapping of inferior and superior disc RNFL quadrants, with average total deviation for corresponding superior and inferior field regions. An SLP or OCT region was considered reduced if a value was.

Results:
At presentation: 9 eyes had superior quadrant SLP reduced, all of which had inferior field loss that did not recover; 4 eyes had inferior quadrant SLP reduced, 3 of which had superior field loss. In contrast, all eyes had a swollen OCT RNFL. At presentation, average SLP superior (48μm) and inferior (54μm) quadrants were significantly worse in eyes with loss in corresponding field regions compared with normal eyes (superior 69μm; inferior 73μm). Baseline superior and inferior field thresholds correlated with corresponding (r=0.39) SLP, but not with OCT, quadrant values. Reduced baseline SLP superior and inferior quadrants correlated with 3-6 month regional OCT thinning (r=0.49) and field loss (r=0.64).

Conclusions:
The RNFL is frequently diminished by SLP, in the regions corresponding to visual field loss acutely in eyes with NAION. Since the visual fields show no notable recovery, SLP loss of birefringence seems to be an early marker for axonal injury.

References:

Keywords: Optical Imaging, NAION, Scanning Laser Polarimetry, OCT, Birefringence

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Tuesday, February 12, 8:30 - 8:45 a.m.

The Ganglion Cell Layer Across the Vertical Meridian in Hemianopsia: I Get No Respect!

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Introduction:
Since the vertical midline is respected in classic homonymous (HH) and bitemporal hemianopsia (BH), resulting loss of retinal ganglion cells should also stop at the vertical meridian in lesions of the optic tract or chiasm. However, anatomic labeling studies demonstrate retinal ganglion cell (RGC) soma located in the hemiretina that show “spill-over” across the vertical meridian (1,2,3). Spectral domain optical coherence tomography (SD OCT) was used to analyze whether the distribution of loss in the macula crosses this anatomic threshold in such patients.

Methods:
12 eyes (6 patients) with HH and 15 eyes (11 patients) with BH on kinetic and standard automated perimetry underwent fields and macular SD OCT on the same day. Probability maps of the ganglion cell layer plus inner plexiform layer (GCIPL) were analyzed for horizontal extent of thinning beyond the vertical meridian, corresponding to the normal visual hemifield. Extent was measured in millimeters (mm) and degrees (deg), with thinning measured at the 5% level of the normative database.

Results:
Mild spill-over of GCIPL thinning into the seeing hemifield was observed in 12 HH eyes (0.41± 0.29 mm, 1.42±1.00 deg) and in 4 BH eyes (0.77±0.27mm, 2.67±0.96 deg). However, 11 BH eyes showed marked spill-over of GCIPL thinning into more of the temporal retina despite midline-respecting visual field defects (1.96±0.44 mm, 6.84±1.53 deg). In total, BH eyes had a significantly greater GCIPL thinning in the seeing hemifield than HH eyes, 1.87mm (6.53 deg) vs. 0.41mm (1.42 deg), respectively (p<0.01, Mann-Whitney Rank Sum Test).

Conclusions:
With visual field defects respecting the vertical meridian, homonymous hemianopsia-producing tract lesions show mild spill-over of ganglion cell loss across the vertical meridian, consistent with anatomic RGC overlap in the retina. However, most eyes with bitemporal hemianopsia demonstrate much greater GCIPL spill-over, suggesting atrophy of non-crossing axons that is not apparent on visual field testing.

References:

Keywords: OCT, Bitemporal, Hemianopsia, Retinal ganglion cell, Vertical Meridian

Financial Disclosures: The authors had no disclosures.
SIRT1 Reduces Oxidative Stress and Delays RGC Loss Following Optic Nerve Crush

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Introduction:
SIRT1 activation prevents loss of retinal ganglion cells (RGCs) in experimental optic neuritis. While the mechanism of this effect is unknown, a role in reduction of oxidative stress has been suggested. Because oxidative stress is a common mechanism of neuronal damage, we hypothesized that SIRT1 may reduce RGC loss due to oxidative stress following traumatic injury.

Methods:
Optic nerve crush injury was induced in wild-type C57/Bl6 mice as well as mice overexpressing SIRT1, and mice with a conditional knockdown of SIRT1 in neurons. Wild-type control and optic nerve crush mice were treated daily with vehicle or 250 mg/kg resveratrol, a naturally-occurring polyphenol that can activate SIRT1. Visual function was assessed by pupillometry and optokinetic responses (OKR), and RGC survival was measured by counting fluorogold labeled cells. Accumulation of the reactive oxygen species superoxide was measured by MitoSOX Red staining to assess oxidative stress.

Results:
Optic nerve crush induced significant decreases in pupillary light responses, OKR and RGC survival one week after optic nerve crush, with progressive worsening at 2-4 weeks. Overexpression of SIRT1 and treatment with resveratrol delayed loss of vision and RGCs following optic nerve crush, and increased RGC loss occurred in neuronal SIRT1-deficient mice. MitoSOX Red staining showed accumulation of superoxide in wild type optic nerves following crush, and was reduced in mice overexpressing SIRT1 or treated with resveratrol.

Conclusions:
SIRT1 delays RGC loss following traumatic injury, similar to its ability to prevent RGC loss during optic neuritis. Effects are likely due to reduced oxidative stress. Results suggest SIRT1 activating drugs may have a specific role in preventing traumatic optic nerve damage, and suggest a broader role for this strategy in treating a wide variety of optic neuropathies that may include a component of oxidative stress.

Keywords: Neuroprotection, Resveratrol, Oxidative Stress, Retinal Ganglion Cells, Traumatic Optic Neuropathy

Financial Disclosures: The authors had no disclosures.
Finite Element Modeling of Chiasmal Compression: Nearer to an Understanding of Bitemporal Hemianopia?

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1Department of Neurology, The Canberra Hospital, Canberra, Australia, 2Australian National University Medical School, Canberra, Australia, 3School of Engineering and Information Technology, University of New South Wales, Canberra, Australia, 4Department of Ophthalmology, Belfast Health and Social Care Trust, Belfast, United Kingdom, 5Queen's University, Belfast, United Kingdom

Introduction:
The precise mechanism of bitemporal hemianopia (BH) in the context of chiasmal compression is unknown. Previous theories have suggested that the blood supply of the crossing fibres is selectively compromised [1] or that crossing fibres are vulnerable because they occupy the centre of the chiasm where the highest pressures occur [2]. We have previously proposed that BH arises because crossing fibres are more vulnerable to compression simply because they cross each other [3]. The current study used finite element modelling (FEM) to explore this question further.

Methods:
A geometric model of the chiasmal sheath, optic nerve fibres and tumorous pituitary gland was constructed in an FEM software package using material properties derived from the literature. The distribution of internal pressure (stress) and deformation (strain) in the chiasm were calculated as a function of pituitary growth. Further modeling was performed to investigate the differential effect of pressure on fibres which did or did not cross.

Results:
Compression of the optic chiasm gave rise to greater stress at the centre of the chiasm than at the periphery (see figure). Crossing fibres were subject to significantly greater stress than parallel fibres. Results from the model were consistent with the few existing measurements from cadaveric and animal studies.

Conclusions:
The numerical consistency with previous studies suggests that FEM is an appropriate tool. The difference in pressure between the centre and the periphery of the deformed chiasm does not explain the “step” at the vertical meridian, i.e. the “respect for the midline”, observed clinically. The current study has shown that the “step” can be explained by incorporating the effect of nerve fibre crossing into the model. BH may ultimately be the end result of a combination of several factors.

References:


Keywords: Optic Chiasm, Bitemporal Hemianopia, Finite Element Modeling, Chiasmal Compression, Pituitary Tumor

Financial Disclosures: The authors had no disclosures.
Tuesday, February 12, 10:00 - 10:15 a.m.

Hand-Held Optical Coherence Tomography During Sedation Detects Visual Acuity and Visual Field Loss in Young Children with Optic Pathway Gliomas

Robert A. Avery1, Eugene I. Hwang1, Hiroshi Ishikawa2, Maria T. Acosta1, Kelly A. Hutcheson1, Domiciano Santos1, Dina J. Zand1, Lindsay B. Kilburn1, Kenneth N. Rosenbaum1, Brian R. Rood1, Joel S. Schuman2, Roger J. Packer1

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Introduction:
To remedy the difficulty in acquiring peripapillary retinal nerve fiber layer (RNFL) measures in young children with optic pathway gliomas (OPGs), we performed hand-held optical coherence tomography (HH-OCT) during sedation. We hypothesize that children who have experienced visual acuity (VA) and visual field (VF) from their OPG will have reduced RNFL thickness.

Methods:
A cross-sectional analysis of children with OPGs enrolled in a prospective study of HH-OCT was performed. Subjects were included if they were cooperative for VA testing and completed HH-OCT under sedation for their clinically indicated magnetic resonance imaging. One-way analysis of variance and a generalized estimating equation approach to variance estimation was used to determine the unadjusted and adjusted associations of clinical variables on the relationship between vision outcomes and RNFL (microns).

Results:
Thirty-two children with OPGs were included for a total of 61 study eyes (median age = 4.86 years, range, 1.8-12.6). RNFL thickness was decreased in the abnormal VA (83.15 ± 12.80), abnormal VF (93.80 ± 20.59) and abnormal VA/VF (65.80 ± 15.70) groups compared to the normal VA/VF group (125.76 ± 14.34; F = 35.89, p <0.0001). In unadjusted and adjusted regression models, RNFL thickness had a strong relationship to VA (p <0.0001) that was not influenced by patient age, diagnosis of neurofibromatosis type 1 or tumor location (optic nerve, chiasm, or tracts).

Conclusions:
HH-OCT measures of RNFL thickness have a close relationship to both VA and VF loss in young children with OPGs. For young children who do not cooperate with VA or VF testing, HH-OCT measures may be a surrogate marker of visual pathway integrity.

Keywords: Optic Pathway Glioma, Optical Coherence Tomography, Visual Acuity, Pediatrics

Financial Disclosures: This project was supported in part by the Children's Tumor Foundation "Clinical Research Award" (Dr. Avery), the National Eye Institute/National Institutes of Health grants K23 EY022673 (Dr. Avery) and R01-EY013178 (Drs. Ishikawa and Schuman), the National Institutes of Health/National Eye Institute Pediatric Research Loan repayment program (Dr. Avery), and the Gilbert Family Neurofibromatosis Institute (Drs. Avery, Acosta and Packer). Financial Disclosures: Dr. Schuman receives royalties for intellectual property licensed by Massachusetts Institute of Technology to Carl Zeiss Meditec.
Fusion Influences the Bielschowsky Head Tilt Test in Superior Oblique Paresis

Kristina Irsch, Howard S. Ying, David L. Guyton

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Introduction:
To investigate how fusion influences the Bielschowsky head tilt test (BHTT) in unilateral superior oblique paresis (SOP).

Methods:
In eight fusing patients, we correlated haploscopic\textsuperscript{1,2}-determined fusional mechanisms with BHTT differences (BHTTD).

Results:
Five patients used the vertical recti for vertical fusional vergence and showed a mean BHTTD ± SD of 22.2 ± 8.1 PD. After a 30-minute patch test one of those (the only one in whom the test was performed) showed a decrease of 1 PD in BHTTD. Two patients used the “paretic” superior oblique muscle (SOM) and the contralateral superior rectus muscle (SRM) to fuse, and had a mean BHTTD ± SD of 5.5 ± 7.8 PD. The BHTTD of one of these, in whom a patch test was performed, increased by 11 PD. The remaining patient used the oblique muscles (“paretic” SOM and contralateral inferior oblique muscle (IOM)) to fuse, and showed a BHTTD of only 3 PD, increasing to 21 PD after patching. One explanation for this behavior in the last patient involves lingering vergence adaptation of the “paretic” SOM and contralateral IOM, which makes these muscles more effective when activated on ipsilateral head tilt, lessening the expected increase in hyperdeviation. Similarly, in our two patients with oblique/rectus-mediated fusion, the vergence-adapted “paretic” SOM and contralateral SRM are activated on ipsilateral and contralateral head tilt respectively, lessening the hyperdeviation in both directions. In the other five patients, however, the vergence-adapted ipsilateral inferior rectus muscle and contralateral SRM are activated on contralateral tilt, possibly accentuating the BHTTD.

Conclusions:
Fusion influences the BHTTD. The absence of a positive BHTT should not be relied upon to rule out the diagnosis of SOP. In suspected SOP patients with fusion, performing the BHTT after a patch test may be necessary to bring out the BHTTD to support the diagnosis.

References:

Financial Disclosures: The authors had no disclosures.
Tuesday, February 12, 10:30 - 10:45 a.m.

Extraocular Muscle Atrophy and Central Nervous System Involvement in Chronic Progressive External Ophthalmoplegia – A Structural and Spectroscopic Magnetic Resonance Study

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Introduction:
Chronic progressive external ophthalmoplegia (CPEO) is a classical mitochondrial ocular disorder characterized by bilateral progressive ptosis and ophthalmoplegia. These ocular features can develop either in isolation or in association with other prominent neurological deficits (CPEO+). Molecularly, CPEO can be classified into two distinct genetic subgroups depending on whether patients harbor single, large-scale mitochondrial DNA (mtDNA) deletions or multiple mtDNA deletions secondary to a nuclear mutation disrupting mtDNA replication or repair. The aim of this magnetic resonance imaging study was to investigate whether the ophthalmoplegia in CPEO is primarily myopathic in origin or whether there is evidence of contributory supranuclear pathway dysfunction.

Methods:
Ten age-matched normal controls and twenty patients with CPEO were recruited: nine patients with single, large-scale mtDNA deletions and eleven patients with multiple mtDNA deletions secondary to mutations in POLG, PEO1, OPA1, and RRM2B. All participants underwent a standardized brain and orbital imaging protocol, together with proton magnetic resonance spectroscopy in two voxels located within the parietal white matter and the brainstem.

Results:
There was evidence of significant extraocular muscle atrophy in patients with single or multiple mtDNA deletions compared with controls. There was a high degree of correlation between the two eyes of the same patient for these atrophic muscle changes. The reduction in extraocular muscle volumes was not associated with any specific high-signal imaging abnormalities within the muscle belly. There was no significant difference in metabolite concentrations between the patient and control groups in both the parietal white matter and brainstem regions. Volumetric brain measurements revealed marked cortical and cerebellar atrophy among patients with CPEO+ phenotypes, consistent with the more severe neurological complications that develop in this group of patients.

Conclusions:
The results of this study support a primary myopathic aetiology for the progressive restriction of eye movements that develops in CPEO.

References:

Keywords: Chronic progressive external ophthalmoplegia, Extraocular muscles, Magnetic resonance spectroscopy, Mitochondrial disorders

Financial Disclosures: The authors had no disclosures.
The Light Induced Electromyogram Shows Exaggerated Responses in Patients with Photo-sensitivity

Randy Kardon¹, Andrew Russo, Pieter Poolman, Susan Anderson, Jan Full

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Introduction:
Photosensitivity is prevalent in patients with migraine and traumatic brain injury and can be debilitating, yet the cause is unknown. Currently there is no objective way diagnose it or monitor the effectiveness of treatment. The purpose of this study was to determine if the photic-electromyogram (photic-EMG), an objective test of light sensitivity, shows an exaggerated response in photo-sensitive patients with either a history of migraine or traumatic brain injury, compared to normal subjects.

Methods:
11 patients with symptoms of photo-sensitivity (8 with a history of migraine but without headache at the time of testing and 3 with a history of traumatic brain injury) and 12 normal subjects were tested using red (640nm) and blue (485nm) Ganzfeld, full field light, one second in duration, over a 6 log unit range of intensity (0.5 log unit steps). Time-stamped, computerized recordings of the orbicularis and procerus/corrugator muscle EMG were quantified and the maximum root mean squared (RMS) of the EMG relative to baseline was compared between the patients and age matched control subjects. Calcitonin Gene Related Peptide (CGRP) was also measured from saliva swabs before, during, and after light stimuli.

Results:
Subjects with photosensitivity had a 4.8 fold (migraine) and 4.4 fold (TBI) increase in photic-EMG response relative to baseline EMG activity to increasing light intensities compared to a 2.5 fold increase in normal subjects (p<0.002). Calcitonin levels in saliva were also increased in photosensitive patients after light stimulation relative to control subjects.

Conclusions:
This pilot study demonstrated that the photic-EMG shows a significant exaggerated response in subjects with migraine or TBI with light sensitivity. The light induced EMG of the orbicularis and procerus/corrugator muscles shows promise as a useful objective test for diagnosis and classification of migraine patients and patients with other causes of light sensitivity and for monitoring their response to individualized treatment.

Keywords: Photosensitivity, Electromyogram, Traumatic brain injury, Migraine

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Leber Hereditary Optic Neuropathy G11778A Gene Therapy Clinical Trial: Stability of Clinical Parameters in Preparatory Phase Based on Onset of Visual Loss

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Introduction:
The preparatory phase of the LHON gene therapy trial aims to characterize affected patients and carriers for the planned gene therapy study that will utilize “alloptopic expression” via an adeno-associated virus vector. We have followed the natural history of affected patients to characterize visual function outcome variables for the planned phase I and II studies.

Methods:
LHON patients with acute or chronic visual loss and their asymptomatic maternally-related relatives undergo ocular examination, visual fields, pattern electroretinogram (PERG), spectral-domain OCT and fundus photography every 6 months.

Results:
105 persons with G11778A have been recruited since 2008. 44 affected patients and 45 asymptomatic carriers have returned for one or more follow-up visits (6 to 36 months). 7 eyes of 6 (14%) patients, all with ≤36 months since initial acuity loss, recovered 15 or more ETRDS letters; however, recovery to >70 total letters was rare (4%) in patients with >12 months since onset. Acuity recovery, when it occurred, happened despite prior marked RNFL thinning (to mean=66um). Asymptomatic carriers had a small 4 letter deficit in acuity compared to the unaffected eyes of ONTT patients at baseline (p=0.009), but did not lose acuity during follow-up. Carriers did lose PERG amplitude over follow-up (p<0.001).

Conclusions:
For affected LHON patients, clinical measures were stable during follow-up, and spontaneous improvement to >70 ETDRS letters was rare (<5%) in chronic patients, making gene therapy improvements with injection of AAV containing a normal ND4 easy to detect. In chronic patients, effectiveness of a therapy with 95% efficacy could be established with 6 patients in an uncontrolled phase II study. For carriers, the PERG amplitudes continue to decrease in year two suggesting subclinical retinal ganglion cell dysfunction.

References:


Keywords: Leber hereditary optic neuropathy, Gene therapy

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Functional Connectivity in Patients with Clinically Isolated Optic Neuritis

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Introduction:
Optic neuritis (ON) is common in MS¹, and visual dysfunction is a major cause of disability in MS patients. Conventional magnetic resonance imaging (MRI) techniques show only a loose correlation between MRI lesion burden and disability in MS, and do not capture physiologic response by the brain to injury². Resting state functional MRI (rs-fMRI) is a novel method of assessing functional connections in the brain by exploring correlations in blood oxygen level dependent (BOLD) fluctuations throughout the brain³,⁴, and represents a promising technique for exploring changes in brain functional connections.

Methods:
We evaluated 9 patients with isolated optic neuritis and no history of MS using rs-fMRI within six weeks of symptom onset. Matched controls also underwent rs-fMRI imaging. Using a seed based method, cross correlation matrices were obtained for 6 mm regions of interest (ROI) within the visual system including bilateral V1, bilateral middle temporal (MT), and bilateral frontal eye fields (FEF).

Results:
Decreases in connectivity were observed between left and right primary visual cortex (p=.049) as well as right and left frontal eye field connectivity (p=.006) for ON subjects compared to controls. No differences were observed in functional connectivity between ipsilateral V1 and MT areas on the right or left for subjects compared to controls (p>.07). There was an increase in functional connectivity within the default mode network (DMN) in ON subjects compared with controls.

Conclusions:
Our findings suggest that inflammatory injury to the optic nerve may lead to changes in functional connections within cortical regions devoted to vision. We also detected increased connectivity in the Default Mode Network (a brain network active at rest)⁵. It remains unclear whether the increased connectivity represents a compensatory mechanism occurring as a result of injury. The visual system may be an ideal model to study functional changes in the brain in patients with early demyelination.

References:

Keywords: Functional MRI, Optic neuritis, Multiple sclerosis, Demyelination, Neuroimaging

Financial Disclosures: The authors had no disclosures.
Tuesday, February 12, 11:30 - 11:45 a.m.

**Functional Burden of Strabismus: Decreased Binocular Summation (BiS) and Binocular Inhibition**

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**Introduction:**
Binocular summation (BiS), defined as the superiority of visual function for binocular over monocular viewing, decreases with age and large interocular differences in visual acuity (VA). In extreme cases, patients may have binocular inhibition whereby their binocular vision is worse than that of their better eye alone. BiS has not been well-studied as a functional measure of binocularity in strabismus. Additionally, there are multiple subjective complaints in strabismus patients that are not easily explained by current knowledge of their binocular function. We hypothesized that strabismus patients may have diminished BiS and perhaps binocular inhibition.

**Methods:**
Strabismus patients and normal controls prospectively underwent a battery of psychophysical and electrophysiological tests including Early Treatment of Diabetic Retinopathy Study Visual Acuity (ETDRS VA), Sloan low contrast acuity (LCA, 2.5%, 1.25%), Pelli-Robson contrast, and sweep visual evoked potential (sVEP) contrast sensitivity to determine BiS for each. BiS was calculated as the ratio between binocular and better eye scores.

**Results:**
Sixty strabismic and 80 normal subjects were prospectively examined (age range 8-60 years). Mean BiS was significantly lower in the strabismic patients than controls for the LCA charts (2.5% and 1.25%, p<0.0001 for both). For 1.25% LCA, strabismics had a mean BiS score<1, indicating binocular inhibition. There was no significant BiS on the ETDRS, Pelli-Robson or sVEP contrast threshold test. Regression analysis revealed a significant association between BiS and strabismus for 2.5% (p<0.0001) and 1.25% (p<0.0001) LCA accounting for age and interocular difference in VA.

**Conclusions:**
BiS is significantly decreased in strabismus, and at the lowest contrast, two misaligned eyes viewing were worse than monocular viewing alone, suggesting that strabismus impairs visual function more than previously appreciated. This may explain why non-diplopic strabismic patients close one eye in visually-demanding situations. This represents an advancement in understanding of the visual deficits in strabismus and suggests that BiS may represent a novel measure to evaluate and monitor binocular function.

**Keywords:** Strabismus, Binocular vision, Binocular summation

**Financial Disclosures:** The authors had no disclosures.
Surgical Outcomes in Adult Sixth Nerve Palsy

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Introduction:
Sixth nerve palsy (6NP) is the most common adult ocular motor nerve palsy. Our goal was to identify factors associated with surgical outcomes in 6NP.

Methods:
Medical records of all adult patients from 1988-2012 with 6NP who underwent strabismus surgery or botulinum toxin injections were retrospectively reviewed. Success was defined as absence of diplopia without prisms, vertical deviation ≤3°, and horizontal deviation ≤10PD.

Results:
83 patients from four surgeons were included [50 (60%) women; mean age 52 (range: 20-86)]. 66 (80%) had unilateral 6NP. Palsies were complete in 34 (41%). 21 (25%) had >1 surgery. Underlying etiology was idiopathic/microvascular in 23 (28%), traumatic in 23 (28%), neoplastic in 19 (23%), and miscellaneous causes in 18 (22%). Success frequency was similar across etiologies. 16/42 patients (38%) with trauma or neoplasm required >1 surgery vs. 5/41 (12%) with other etiologies (p<0.05). Partial 6NP trended toward better success than complete 6NP (33/49=67% vs. 16/34=47%;p=0.065). Patients undergoing botulinum toxin injections alone (10/83=12%) had a success rate of (6/10=60%). Success was more frequent with Hummelsheim-type procedures than vertical rectus transposition (VRT) among patients with complete palsies (7/9=78% vs. 8/23=35%;p<0.05). Success was more frequent with adjustable vs. nonadjustable sutures for all 6NP (21/29=73% vs. 22/44=52%;p=0.06). Patients had similar rates of reoperation with adjustable and nonadjustable sutures (8/29=31% vs. 8/44=18%;p=0.20).

Conclusions:
Anatomical and sensory surgical success for 6NP in adults may vary based on the type of procedure used, with Hummelsheim-type procedures for complete 6NP and adjustable sutures for all 6NP resulting in more successful outcomes. Etiology of 6NP does not appear to affect ultimate surgical success in adults, but patients with traumatic and neoplastic causes are more likely to require repeat procedures.

Keywords: Adult Strabismus, Sixth Nerve Palsy, Surgery

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