Platform Session II  
Pacific Ballroom  
Tuesday, February 8, 2011  
7:30 a.m. – 12:00 p.m.

Moderators: Fiona Costello, MD, FRCP and Howard Pomeranz, MD, PhD – before break  
Moderators: Marie Acierno, MD and Wayne Cornblath, MD – after break

7:30 a.m. - 7:45 a.m.  Randy Kardon
The Light Induced Electromyogram (EMG): A Reflex Pathway Integrating the Melanopsin Retinal Ganglion Cell, Trigeminal Sensory Nucleus and Facial Nerve

7:45 a.m. - 8:00 a.m.  Jonathan Horton
Color Versus Form: Orientation Tuning of Cytochrome Oxidase (CO) Patches in Macaque Primary Visual Cortex Explored with 100-Microelectrode Recording Arrays

8:00 a.m. - 8:15 a.m.  Jennifer Graves
Visual Pathway Axonal Loss in Patients with Benign Multiple Sclerosis

8:15 a.m. - 8:30 a.m.  Mark Kupersmith
Optical Coherence Tomography of the Swollen Optic Nerve Head: Deformation of the Peripapillary RPE Layer in Papilledema

8:30 a.m. - 8:45 a.m.  Celia Chen
Efficacy of Intravenous Tissue Plasminogen Activator in Central Retinal Artery Occlusion: Report from a Randomized Controlled Trial

8:45 a.m. - 9:00 a.m.  Marie D. Acierno
Rescue Therapy for Malignant Idiopathic Intracranial Hypertension

9:00 a.m. - 9:15 a.m.  Michael Wall
The Effect of Stimulus Size on Repeatability using Goldmann Sizes III, V, and VI: Size Matters

9:15 a.m. – 10:00 a.m.  JNO Update/Coﬀee Break

10:00 a.m. - 10:15 a.m.  Rebekah Ahmed
Management of Idiopathic Intracranial Hypertension (IIH) with Stenting of Transverse Sinus Stenoses

10:15 a.m. - 10:30 a.m.  Brian Younge
Evolution of Vascular Arteritis: A Pilot Study

10:30 a.m. - 10:45 a.m.  Safinaz Mostafa
Interaction of Sex Hormones and Genetics in the Pathogenesis and Prevention of Dry Eye in Sjögren’s Syndrome
10:45 a.m. - 11:00 a.m.  Robert Avery
Cerebrospinal Fluid Opening Pressure in Children with Optic Nerve Head Edema: A Case-Control Study

11:00 a.m. - 11:15 a.m.  Bradley Katz
Identification of Burkholderia in the Temporal Arteries and Blood of Patients with Giant Cell Arteritis

11:15 a.m. - 11:30 a.m.  Mohammad Fouladvand
Pipeline Embolization Device (PED) in the Treatment of Complex Large and Giant Aneurysms of the Internal Carotid Artery (ICA): Effect on Visual Symptoms and Neuro-ophthalmologic Outcome

11:30 a.m. - 11:45 a.m.  Grant Liu
Pseudotumor Cerebri due to Recombinant Human Insulin-like Growth Factor (rhIGF-1)

11:45 a.m. - 12:00 p.m.  Ewa Niechwiej-Szwedo
The Effects of Anisometropic Amblyopia on Saccadic Eye Movements
7:30 a.m. - 7:45 a.m.

The Light Induced Electromyogram (EMG): A Reflex Pathway Integrating the Melanopsin Retinal Ganglion Cell, Trigeminal Sensory Nucleus and Facial Nerve

Randy Kardon, Pieter Poolman

1University of Iowa, Department of Ophthalmology and Visual Sciences, Iowa City, Iowa, United States, 2Department of Veterans Affairs, Center of Excellence for the Prevention and Treatment of Visual Loss, Iowa City, Iowa, United States

Introduction:
The Photo-Blink Reflex protects the eye after a bright flash of light (1-4). Melanopsin containing retinal ganglion cells may comprise the afferent arm of this reflex through projections to the trigeminal nucleus (5) and may explain the paradoxical photosensitivity in patients blinded by photoreceptor loss (5). To characterize this reflex, the EMG, pupil movement and skin conductance were recorded to increasing red and blue light stimuli.

Methods:
Five subjects were tested under both scotopic and photopic conditions using red (640nm) and blue (485nm) Ganzfeld light one second in duration over a 6 log unit range of intensity (0.5 log unit steps). Time-stamped, computerized recording of the pupil, orbicularis and procerus muscle EMG, and skin conductance were measured simultaneously.

Results:
The EMG showed a linear increase with log unit light intensity in parallel with pupil responses, but with a threshold approximately 3 log units less sensitive. At the brightest light intensities, an involuntary reflex blink was also triggered. Similar to pupil responses, the EMG showed a sustained, prolonged response to bright blue light stimuli, consistent with intrinsic activation of melanopsin containing retinal ganglion cells. Subjects with the largest light-induced EMG responses also had the largest changes in skin conductance.

We provide the first physiological evidence in humans that the light induced EMG response is mediated by melanopsin containing retinal ganglion cells, providing input to the trigeminal sensory nucleus, which then stimulates efferent output from the facial nucleus (as evidenced by EMG responses of orbicularis and procerus muscles) and sympathetic nervous system (as evidenced by increases in skin conductance). This unique light reflex may be useful in monitoring afferent light input affected by retinal and optic nerve disorders and also in diagnosing photosensitivity due to either ocular or central causes.

References:

Key Words: Electromyogram EMG, Trigeminal Reflex, Melanopsin Retinal Ganglion Cells, Pupil Light Reflex, Sympathetic Nerve

Financial Disclosure: None
Introduction:
Livingstone and Hubel reported that cells within CO patches are specialized for processing color, and therefore lack tuning for the orientation of a stimulus. We studied the properties of CO patches by using a 10 x 10 array of microelectrodes mounted onto a miniature chip. This device allows one to record from many neurons simultaneously and permits histological localization of each recording site in the cortex.

Methods:
Electrode arrays were implanted into V1 of anesthetized monkeys using a high speed pneumatic inserter, aiming to sink the tips into layer 3. The aggregate receptive field was stimulated with drifting achromatic sine-wave gratings, randomly interleaved over a range of orientations and spatial frequencies. After the recordings, animals were perfused and striate cortex was processed to pinpoint the location of each electrode tip with respect to CO patches.

Results:
Eight array implantations in 5 macaques yielded recordings in layer 3, where CO patches are most visible. Orientation tuning profiles were compiled for the cells isolated at each electrode. The circular variance, a measure of orientation tuning, was calculated for each cell (0 = perfectly tuned, 1 = untuned). Each cell was assigned to a patch or interpatch, depending on the density of CO activity at the electrode tip. A wide range of circular variances was found in patches (mean 0.64, n = 173) and interpatches (mean 0.54, n = 434). Cells in patches were slightly less well tuned for orientation than cells in interpatches (p < 0.001, Wilcoxon rank sum).

Conclusion:
Patches are less tuned for orientation than interpatches, but they still contain many well oriented cells. This finding suggests that patch cells contribute to the perception of form, in addition to color. The segregation of color and form must occur at a higher level in the visual system.

References:

Key Words: Cytochrome Oxidase Patch, Orientation Tuning, Macaque Striate Cortex, Color Vision, Microelectrode Array

Financial Disclosure: None
8:00 a.m. - 8:15 a.m.

Visual Pathway Axonal Loss in Patients with Benign Multiple Sclerosis

Jennifer Graves1, Kristin Galetta1, Lauren Talman1, Deacon Lile1, Stephanie Syc3, Amy Conger2, Gina Remington2, Peter Calabresi2, Elliott Frohman2, Steven Galetta1, Laura Balcer1

1University of Pennsylvania, Philadelphia, PA, United States, 2University of Texas Southwestern, Dallas, TX, United States, 3John Hopkins, Baltimore, MD, United States

Introduction:
Benign MS, defined most often as EDSS score ≤3 with ≥15 years’ disease duration, is traditionally thought to follow a milder course. Recent work suggests that axonal loss and disease progression occur even in this group of patients with mild impairment. We examined the extent of visual pathway axonal loss and visual disability in a benign MS cohort.

Methods:
Patients were participants in an ongoing longitudinal study at three centers. High and low contrast acuity charts were used to test vision. Retinal nerve fiber layer (RNFL) thickness was measured using time- and Fourier-domain OCT. The NEI-VFQ-25 questionnaire was used to assess vision-specific quality of life (QOL).

Results:
Among 70 patients (135 eyes) studied longitudinally, 19 had benign MS using EDSS ≤3 and ≥15 years’ disease duration. Age (51±5 vs. 49±8 years), visual function, RNFL thickness, and follow-up in study (1.7 vs. 1.3 years) were similar for benign vs. typical MS. Benign MS eyes had as much RNFL thinning from baseline (-4.2 microns, p<0.0001 vs. baseline) as did typical MS eyes (-3.0 microns, p<0.0001). Both groups had significant low-contrast acuity loss over time. Prior history of optic neuritis (ON) was more frequent in benign MS eyes (63% vs. 30%). History of ON distinguished benign vs. typical MS (p=0.002) and correlated with RNFL thinning (p=0.01) and disease duration (p=0.03), but not with EDSS (p=0.32). NEI-VFQ-25 scores were worse for benign MS at follow-up compared to typical MS (78±21 vs. 88±11, p=0.004, accounting for age).

Conclusion:
Patients with benign MS have anterior visual pathway axonal loss similar to that of typical MS, and have reduced vision-specific QOL. Prior ON was twice as frequent in the benign MS group. These results suggest that while overall neurologic impairment is mild, visual dysfunction, not well-captured by the EDSS, accounts for a substantial degree of disability in benign MS.

References: None

Key Words: Multiple Sclerosis, Optical Coherence Tomography, Quality Of Life, Optic Neuritis, Axonal Degeneration

Financial Disclosure: Dr. Gina Remington has received honoraria from Biogen and Teva.

Dr. Peter Calabresi has served on the advisory boards or consulted for Biogen Idec, Genetech, Serono, Teva, Novartis, Eisai, Vertex, and Ampimmune.

Dr. Frohman has been a speaker for or received consulting fees for Biogen Idec, Teva, Athena, and Abbott Laboratories.

Dr. Laura Balcer has received honoraria from Biogen-Idec and Bayer.

Dr. Steven Galetta has received honoraria from Biogen-Idec and Teva.
Optical Coherence Tomography of the Swollen Optic Nerve Head: Deformation of the Peripapillary RPE Layer in Papilledema

Mark Kupersmith¹, Patrick Sibony², Gary Mandel¹, Mary Durbin³, Randy Kardon¹

¹NYEEI, Roosevelt Hospital, NYC, NY, United States, ²SUNY Stony Brook, Stony Brook, NY, United States, ³Zeiss-Meditech, Inc, Dublin, CA, United States, ⁴University of Iowa and VA Medical Center, Iowa City, IA, United States

Introduction:
We examined the biomechanical deformation of load bearing structures of the optic nerve head (ONH) resulting from raised intracranial pressure, using high resolution, spectral domain optical coherence tomography (HD-OCT). We postulated that elevated intracranial pressure induces forces in the retrolaminar subarachnoid space that can deform ONH structures, particularly the peripapillary Bruch’s membrane (BM) and retinal pigment epithelium (RPE) layers.

Methods:
We compared HD-OCT optic nerve and peripapillary retinal nerve fiber layer (RNFL) findings in eyes with papilledema due to raised intracranial pressure to findings in eyes with optic disc swelling due to optic neuritis and non-arteritic anterior ischemic optic neuropathy (NAION), conditions without intracranial hypertension. We measured average thickness of the RNFL and the angle of the RPE/BM at the temporal and nasal borders of the neural canal opening. The angle was measured as positive with inward (towards the vitreous) deflection and as negative with outward deflection.

Results:
Of 30 eyes with papilledema, 20 eyes (67%) had a positive RPE/BM rim angle (mean 1.5 degrees for temporal and 2.5 degrees for nasal angles). One of 8 optic neuritis (12%) eyes and 1/12 NAION (8%) eyes had a positive angle deflection. In 5 papilledema eyes the average RNFL significantly increased, 3 of which developed positive RPE/BM angles. On follow up, 22 papilledema eyes had reduction of average RNFL swelling and 17 of these eyes had less positive RPE/BM angulation.

Conclusion:
In papilledema, the RPE/BM is commonly deflected inward, in contrast to eyes with NAION or optic neuritis. The deflection is likely due to elevated pressure in the subarachnoid space, does not correlate with the amount of RNFL swelling, and resolves as papilledema subsides. The amount of deflection is greater than is seen in glaucoma until the latter has significant structural tissue loss.

References: None

Support:
U10 EY017281-01A1, U10 EY017281-01A1S1
VA Rehabilitation Research and Development Division

Key Words: Optic Nerve Head Swelling, Optical Imaging, Papilledema, RPE/Bruch's Membrane, Biomechanical Deformation

Financial Disclosure: None
Efficacy of Intravenous Tissue Plasminogen Activator in Central Retinal Artery Occlusion: Report from a Randomized Controlled Trial

Celia Chen¹, Andrew Lee¹, Bruce Campbell³, Mark Paine², Clare Fraser⁴, John Grigg⁴, Romesh Markus⁵

¹Flinders Medical Center and Flinders University, Adelaide, South Australia, Australia, ²Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia, ³St. Vincent's Hospital Melbourne, Melbourne, Victoria, Australia, ⁴Save Sight Hospital, Sydney, New South Wales, Australia, ⁵St. Vincent's Hospital Sydney, Sydney, New South Wales, Australia

Introduction:
Central retinal artery occlusion (CRAO) results in a sudden, painless loss of vision and bears a poor prognosis with over 80% of affected persons having a final visual acuity of counting fingers or worse. A meta-analysis of all reported cases suggests that vision improvement occurs in 48.5% of patients treated with intravenous thrombolysis. We aim to assess the efficacy of intravenous tissue plasminogen activator (tPA) given within 24 hours of central retinal artery occlusion (CRAO) onset.

Methods:
A randomized controlled trial comparing intravenous tPA vs placebo in CRAO. Between 2008 and 2010, sixteen eligible patients with acute CRAO were randomized to either intravenous tPA or saline placebo infusion. The primary outcome was improvement in Snellen visual acuity (VA) by greater than or equal to 3 lines at 6 months, equating to a ≥0.3 logMAR change in vision.

Results:
There was no difference in VA between placebo and tPA groups at 6 months. Subgroup analysis demonstrated that tPA administered within 6 hours of symptom onset had an improvement in visual acuity (mean logMAR improvement of -1.1). There was one intracranial hemorrhage in the tPA group leading to premature study cessation by the Data Safety and Monitoring Board.

Conclusion:
This study is the first randomized controlled trial of intravenous t-PA versus placebo in the treatment of CRAO that demonstrated the futility of using a 24 hours treatment window. Subgroup analysis suggested a beneficial effect if tPA is administered within 6 hours of CRAO onset. The use of tPA, even in a radiologically normal brain, is not without risk of intracerebral hemorrhage and cannot be recommended in routine clinical practice pending further study of the optimal time window for intervention.

References:

Key Words: Thrombolysis, Artery Occlusion, Randomized Controlled Trial

Financial Disclosure: None
Introduction:
Idiopathic Intracranial Hypertension (IIH) is a disorder of elevated intracranial pressure of unknown cause. The raised pressure on the optic nerves results in papilledema with subsequent visual loss. The first presentation to the medical community for a small percentage of patients is usually sudden, severe headache, profound papilledema and rapid visual acuity and/or visual field loss. These hyperacute or “malignant” cases of IIH require urgent intervention that should include available surgical procedures such as optic nerve sheath fenestration (ONSF), CSF diversion procedures, and even subtemporal decompression. Often, the clinician may not have immediate access to these surgical interventions. Therefore, we suggest that patients with malignant IIH be “rescued” with a combination of high dose intravenous acetazolamide, short-term high dose methylprednisolone, and placement of a lumbar drain.

Methods:
This is a retrospective review of 6 obese female patients who presented to a major academic University Medical Center with hyperacute, malignant IIH. The average BMI was 46. The most common presenting complaints were blurred vision and headache. The average opening pressure was 43cmH2O. Each patient had a lumbar drain placed in combination with high dose acetazolamide and steroids until they could be safely transported for ONSF.

Results:
The continuous lumbar drain stabilized CSF pressure and provided short-term relief for 3 to 4 days prior to surgical decompression of the optic nerves. All patients had expansion of either visual fields or improvement of visual acuity or improvement of papilledema after treatment with lumbar drain placement followed by ONSF.

Conclusion:
Continuous lumbar drain provides more relief than a single lumbar puncture. We suggest that it is best to temporize with a proposed rescue therapy of a lumbar drain in combination with high dose acetazolamide and methylprednisolone until patients can safely receive more definitive surgical intervention.

References: None

Key Words: Malignant Idiopathic Intracranial Hypertension, Optic Nerve Sheath Fenestration, Rescue Therapy, Lumbar Drain

Financial Disclosure: None
The Effect of Stimulus Size on Repeatability using Goldmann Sizes III, V, and VI: Size Matters

Michael Wall\textsuperscript{2}, Carrie Doyle\textsuperscript{1}, Gideon Zamba\textsuperscript{1}, Chris Johnson\textsuperscript{1}

\textsuperscript{1}University of Iowa, Iowa City, IA, United States, \textsuperscript{2}VA Hospital, Iowa City, IA, United States

Introduction:
Automated perimetry is limited by an exponential rise in variability with decreasing sensitivity and a limited effective dynamic range (EDR). We have shown a reduction in variability using the Goldmann size V stimulus\textsuperscript{1-2} with no corresponding reduction in defect detection.\textsuperscript{3} We hypothesized using an even larger stimulus would further reduce retest variability and increase the EDR. Therefore we tested subjects with stimulus sizes III, V and VI using a custom built perimeter modified to produce a size VI stimulus.

Methods:
We tested 70 glaucoma patients with moderate visual field damage twice within one month with Humphrey program 24-2 using stimulus sizes III, V and VI. Point-wise limits of retest variability were established from the empirical 5th and 95th percentiles of the distribution of retest values, stratified by the sensitivity value of the test location at the first test (Fig). The log differences between test and retest values were linearly regressed onto the averages of the two tests to determine the relationship between variability and sensitivity.

Results:
The average sensitivities were size III: 21 ± 4.5 dB; size V sensitivity: 27.6 ± 3.7 dB and size VI: 30.3 ± 3.2 dB. Using floor effect as an index of EDR, the numbers of 0 dB trials were: size III – 391, size V – 76 and size VI – 21; indicating a greater EDR for the larger stimuli. There was increasing variability associated with lower sensitivity but the rise in variability was less with the larger stimulus sizes, with size VI having the least rise (Fig). We found the following correlations: with size III, sensitivity explained 25% of the retest variability (r\textsuperscript{2}); figures for size V and size VI were 13%, and 9%.

Conclusion:
Large-sized conventional perimetric stimuli have a dampened rise in variability with decreasing sensitivity and a greater effective dynamic range. These large stimuli show promise for use in moderate to severe glaucoma and other optic neuropathies.

References:

Key Words: Perimetry, Visual Testing, Visual Field, Optic Neuropathies

Financial Disclosure: None
10:00 a.m. - 10:15 a.m.

Management of Idiopathic Intracranial Hypertension (IIH) with Stenting of Transverse Sinus Stenoses

Rebekah Ahmed¹, Mark Wilkinson¹, Geoffrey Parker¹, Mathew Thurtell¹, Jason Macdonald¹, Rodney Allan¹, Peter McCluskey¹, Victoria Dunne¹, Mark Hanlon¹, Brian Owler², G. Michael Halmagyi¹

¹Royal Prince Alfred Hospital, Sydney, Australia, ²Westmead Hospital, Sydney, Australia

Introduction:
Transverse sinus stenosis (TSS) is common in patients with idiopathic intracranial hypertension (IIH). While the role of TSS in IIH pathogenesis remains controversial, modelling studies suggest that stenting of a TSS with a significant pressure gradient should decrease cerebral venous pressure and thereby reduce intracranial (CSF) pressure, thereby improving symptoms of IIH and reducing papilledema, even when the stenosis is secondary to the intracranial hypertension. We aimed to determine if IIH could be effectively treated by stenting the TSS.

Methods:
We reviewed the clinical, venographic and intracranial pressure data in 43 of our own patients who underwent stenting of a TSS since 2001 for IIH unresponsive to maximum acceptable medical treatment.

Results:
We reviewed our data from 43 patients, who met diagnostic criteria for IIH and had one or more TSS on direct venography with pressure gradient on manometry, before and after endovascular stenting. The mean superior sagittal sinus pressure was 34mmHg (462mmH2O) with a mean TSS gradient of 20 mmHg. The mean lumbar CSF pressure before stenting was 320mmH2O. Stents were placed using an endovascular approach. Length of follow-up ranged from 6 months to 8 years. The TSS pressure gradient was abolished in all patients immediately following stenting. Most patients reported symptomatic improvement within hours. The papilledema resolved in all patients over weeks and 37/43 had a persisting improvement in visual symptoms and visual fields.
In 6 patients symptom relapse was associated with increased venous pressures and recurrent stenosis adjacent to the previous stent. In these cases, insertion of another stent again abolished TSS pressure gradient and improved symptoms.

Conclusion:
These findings suggest a role for transverse sinus stenting, similar to that for CSF shunting, in the management of selected patients with IIH. A randomized controlled study would be required to confirm this.

References: None

Key Words: Idiopathic Intracranial Hypertension, Transverse Sinus Stenting, Papilledema, Headache, Pseudotumor Cerebri

Financial Disclosure: None
Evolution of Vascular Arteritis: A Pilot Study

Brian Younge¹, Cornelia Weyand², Jorg Goronzy², Kevin Rieck¹, Gene Hunder¹, George Bartley¹, Lester Wold¹

¹Mayo Clinic, Rochester, MN, United States, ²Stanford University, Stanford, CA, United States

Introduction:
- Why does giant cell arteritis (GCA) persist for a year or longer despite treatment?
- When does pathology become normal?
- What are cytokines prior to and after corticosteroids?

Methods:
- We recruited 40 IRB approved patients for temporal artery biopsy
- Part of the specimen went to the Rheumatology lab for cytokine analysis
  - Bloods were drawn for analysis of cytokines by flow cytometry
  - Part of the specimen was preserved by embedding the tissue in T and B cell deficient mice.
- Second biopsies were at 4 intervals: 3, 6, 9 or 12 months

Results:
- Biopsies were still positive in 80% at 3 months, 90% at 6, 30% at, and 20% at 12
- The major mediator of inflammation GCA are CD4 T cells.

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Conclusion:
- Arteritis of GCA clears between 9-12 months
- Dendritic cells are the primary antigen-presenting cell
- CD4 T-cells, stimulated by cytokines differentiate into Th17 cells, and this is markedly suppressed by glucocorticoids
- CD4 T-cells that become Th1 cells are not suppressed by glucocorticoids.
- We can use this differential suppression of Th17 and Th1 cells to provide pathogenic clues and potentially design treatments.

References: None

Key Words: Giant Cell Arteritis, CD4 T-Cells, Th1 T Cells, Th17 T Cells, Cytokines

Financial Disclosure: None
Interaction of Sex Hormones and Genetics in the Pathogenesis and Prevention of Dry Eye in Sjögren’s Syndrome

Safinaz Mostafa, Ana Maria Azzarolo

Florida Atlantic University, Boca Raton, Florida 33431, United States

Introduction:
Dry eye disease occurs mainly due to impairment of lacrimal gland function. Our previous study demonstrated that ovariectomy (OVX) significantly increases the rate of apoptosis and activity of cleaved caspase-3 in the lacrimal gland of a genetically predisposed mouse model (NOD.B10.H2β) of Sjögren’s Syndrome (SS) compared to control (C57BL/10) mice. The increases in cell death and caspase-3 activity were progressively higher with time after OVX in NOD.B10.H2β mice. The purpose of the present study was to investigate whether replacement of the sex hormones dihydrotestosterone (DHT) or 17β-estradiol (E2) at physiological doses post-ovariectomy can prevent apoptosis and the increased activity of cleaved caspase-3 in this genetically predisposed mouse.

Methods:
Six weeks old NOD.B10.H2β and C57BL/10 mice were subjected to 4 treatments: Sham, OVX, OVX+DHT and OVX+E2 for 3 different time periods: 3, 7 and 21 days. Subcutaneous DHT or E2 pellets at physiological doses were administered to DHT or E2 treatment groups respectively. At the end of each experimental time interval the lacrimal glands were removed and stained for cleaved caspase-3 and DNA fragmentation followed by quantification of the staining using Image Pro-plus software.

Results:
Treatment with DHT or E2 prevented the increase in DNA degradation and cleaved caspase-3 at 7 and 21 days post-OVX NOD.B10.H2β mice. DHT or E2 treatment showed no significant effect on DNA fragmentation or cleaved caspase-3 at any of the experimental time points studied in the C57BL/10 mice.

Conclusion:
Our results suggest that both genetic predisposition and deficiency of sex hormones play a role in the pathogenesis of dry eye in SS. Replacement of physiological levels of sex hormones (17β-estradiol or dihydrotestosterone) prevents apoptosis in the lacrimal gland. Activation of caspase-3 seems to be the underlying mechanism triggering programmed cell death in the lacrimal gland of this mouse model of SS.

References: None

Key Words: Dry Eye, Sex Hormones, Sjögren’s Syndrome (SS), Apoptosis, Caspase-3

Financial Disclosure: None
10:45 a.m. - 11:00 a.m.

Cerebrospinal Fluid Opening Pressure in Children with Optic Nerve Head Edema: A Case-Control Study

Robert Avery, Daniel Licht, Samir Shah, Jimmy Huh, Jan Boswinkel, Jeffrey Seiden, Michael Ruppe, Rakesh Mistry, Grant Liu

Children's Hospital of Philadelphia, Philadelphia, PA, United States

Introduction:
We previously reported that an abnormal cerebrospinal fluid (CSF) opening pressure (OP) in children was greater than 28 cm H2O. Since elevated intracranial pressure can cause optic nerve head edema (ONHE), we would expect that most patients with ONHE not due to infectious, inflammatory or ischemic conditions would have an OP greater than 28 cm H2O. This study describes the range of OP for children with ONHE and compared them to age-matched controls without ONHE.

Methods:
Case subjects were children (1 – 18 years of age) enrolled in a prospective study of CSF OP that demonstrated ONHE at time of lumbar puncture and that the ONHE later resolved. Patients with ONHE secondary to infectious (e.g., Lyme disease), inflammatory (e.g., sarcoid) or ischemic (e.g., vasculitis) conditions were excluded. Control subjects from the same study, but without ONHE were matched to cases based on age, depth of sedation during lumbar puncture, and body mass index category. The mean OP and distribution was compared between cases and controls.

Results:
Of the 472 subjects enrolled in the study, 41 OP measurements were obtained from 33 patients with ONHE who did not have any exclusionary criteria and matched to 41 control subjects without ONHE. Case subjects had a significantly higher OP (mean, 41.4 cm H2O; range, 22-56) than control subjects (mean, 18.9 cm H2O; range, 9-29; paired t-test p < 0.01). Forty of 41 (97.6%) ONHE cases had OP measurements ≥ 30 cm H2O, compared to none of the control subjects.

Conclusion:
Children with ONHE not related to infectious, inflammatory or ischemic causes typically have an OP ≥ 30 cm H2O, significantly higher than age-matched controls without ONHE. This study provides further support to our previously published findings that suggests an abnormal OP in children is typically above 28 cm H2O.

References:

Key Words: Pseudotumor Cerebri (IIH), CSF opening pressure, Lumbar puncture, Pediatrics, papilledema

Financial Disclosure: None
11:00 a.m. - 11:15 a.m.

Identification of *Burkholderia* in the Temporal Arteries and Blood of Patients with Giant Cell Arteritis


*University of Utah, Salt Lake City, UT, United States*

**Introduction:**
Previous investigators have postulated that an infectious agent causes giant cell arteritis (GCA). Attempts to culture an organism have been unsuccessful. Non-human DNA has been identified in tissue samples, but a causative organism has never been positively identified.

**Methods:**
Patients undergoing superficial temporal artery biopsy (STAB) on suspicion of GCA were invited to participate. Blood samples were obtained and a small segment of the biopsy was preserved and frozen. RNA was isolated and DNA was created by RT-PCR and sequenced. A commercial anti-LPS monoclonal antibody for *Burkholderia* was used for immunohistochemistry and ELISA. *Burkholderia* was cultured in selective media and incubated *in vitro* with murine aortas and bone marrow macrophages.

**Results:**
We identified bacterial 16s ribosomal RNA in the artery walls of 6 patients with GCA. This DNA had 100% homology with a strain of *Burkholderia*. RT-PCR using primers specific for *Burkholderia* confirmed the presence of the organism in 4 of 6 affected arteries and the absence of the organism in 2 unaffected arteries. Immunohistochemistry revealed *Burkholderia* in tissue samples from 4 additional affected subjects; no organisms were detected in samples from 3 additional unaffected subjects. LPS from the bacteria was detectable in the sera of 7 additional affected subjects and not in the sera of 16 additional unaffected subjects. The organism was cultured from affected arteries and incubated *in vitro* with murine aortas and bone marrow macrophages. Murine vascular dendritic cells were activated by the organism and macrophages formed multinucleated giant cells.

**Conclusion:**
Although these results do not definitively prove that GCA is caused by *Burkholderia*, these attributes of this organism, along with our detection of this organism in the blood and tissue of affected subjects, and its absence in unaffected subjects, suggests a strong association of *Burkholderia* with that will require further study.

**References:**

**Key Words:** Giant Cell Arteritis, Temporal Arteritis, Burkholderia, PCR, Immunohistochemistry

**Financial Disclosure:** None
Pipeline Embolization Device (PED) in the Treatment of Complex Large and Giant Aneurysms of the Internal Carotid Artery (ICA): Effect on Visual Symptoms and Neuroophthalmologic Status

Mohammad Fouladvand, Daniel Cher, Tibor Bezcke, Peter Kim Nelson

New York University medical center, New York, United States

Introduction:
Complex aneurysms of the ICA, especially those in the cavernous and paraophthalmic segments, present distinct challenges for definitive parent-vessel sparing neuroendovascular treatment. PED offers a new therapeutic solution for these lesions. PED is a braided, high-coverage, endoluminal implant designed to reconstruct the parent vessel lumen and alter intra-aneurysmal hemodynamics, promoting intra-saccular hemostasis and aneurysm thrombosis without the need for coil embolization. PED may offer improved occlusion rates over conventional stent/coil techniques. Moreover, by averting the need for intraaneurysmal coils, PED may permit more complete resolution of mass effect, with attendant improvement in neurologic symptoms caused by the aneurysm.

Methods:
104 subjects (94F: 10M, mean age 56.8 years) with qualifying large cavernous and proximal supracleinoidal segment carotid aneurysms were treated with PED as part of a prospective, single-arm clinical trial. Each subject underwent neuroophthalmologic evaluation prior to treatment and at 6 months by a neuroophthalmologist. Follow-up angiographic assessment of the aneurysm was obtained at 6 months. As part of evaluation, a single neuroophthalmologist (MF) completed an independent assessment of all study subjects, reviewing clinical examination worksheets and other relevant information.

Results:
Analysis was performed on 98 subjects who had both baseline and follow-up examinations. Ipsilateral visual field abnormalities clearly related to the target aneurysm were present at baseline in 17, of which 9 subjects improved, 7 remained stable and 1 became worse by 180 days. 9 subjects had visual acuity abnormalities related to the target aneurysm, of which 3 had marked improvement, 2 were somewhat improved and 4 were about the same at 180 days. Oculomotor problems related to the target aneurysm were seen in 15 (CN3), 1 (CN4) and 20 (CN6) subjects at baseline. Of those with CN3 abnormalities, 7 were improved and 1 showed complete resolution; of those with CN6 abnormalities, 9 were improved and 5 showed complete resolution. One subject showed cilioretinal artery occlusion and 4 developed new persistent cranial neuropathies.

Conclusion:
PED embolization of complex symptomatic ICA aneurysms results in significant improvements in visual outcomes and neuroophthalmologic function compared to coil-based endovascular therapies.

References: None

Key Words: Internal Cavernous- Carotid Artery Aneurysm, Diplopia, Optic Neuropathy, Pipeline Embolization Device, PUFS Trial

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11:30 a.m. - 11:45 a.m.

Pseudotumor Cerebri Due to Recombinant Human Insulin-Like Growth Factor (rhIGF-1)

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Introduction:
A few isolated cases of pseudotumor cerebri (PTC) due to recombinant human insulin-like growth factor (rhIGF-1), used to treat short stature for instance, have been reported. A systematic review of cases, important to support an association, has not been performed.

Methods:
A retrospective review of cases ascertained from databases of Genentech and Tercica rhIGF-1 clinical trials, IGFD Registry, and spontaneous reports from commercial use was performed. Cases were evaluated whether rhIGF-1 use led to PTC, based upon their temporal relationship and whether the modified-Dandy criteria for the diagnosis of PTC/IIH were met. A qualitative description of the relationship between rhIGF-1 and PTC was assigned (definite, highly highly probable (HHP), highly probable (HP), or probable (P)).

Results:
From 1989-2010, 3793 total patients were treated with rhIGF-1, and 21 cases were identified for further review. Of these, none satisfied all the modified-Dandy criteria, usually because the patients were incompletely evaluated with imaging or lumbar punctures. However in two cases the relationship between rhIGF-1 was HHP, in 7 HP, and in 7 probable. Headache was the most common symptom, and the patient age range was 7-15 years, all were male, and none were obese. In most cases visual function was incompletely assessed. In one the relationship was unlikely, and in 4 there was not enough information. Thus in (2+7+7)=16 patients treated with rhIGF-1 in these databases, there was at least a probable relationship between the drug and PTC. When documented, cessation of rhIGF-1 was sufficient for resolution of PTC.

Conclusion:
The sheer number of HHP, HP, and P cases of PTC which developed during rhIGF-1 use suggests that rhIGF-1 likely is a drug which causes PTC. More careful documentation of cases with regards to imaging, lumbar punctures, and visual assessments, is recommended.

References: None

Key Words: Pseudotumor Cerebri, Idiopathic Intracranial Hypertension, Recombinant Human Insulin-Like Growth Factor (rhIGF-1)

Financial Disclosure: Dr. Liu has received personal compensation for speaking and consulting for Ipsen Pharmaceuticals, but did not receive compensation for performing this study or presenting its findings.
The Effects of Anisometropic Amblyopia on Saccadic Eye Movements

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Introduction:
Impairment of spatiotemporal visual processing is the hallmark of amblyopia, but its effects on eye movements during visuomotor tasks have rarely been studied. Here, we investigate how the visual deficits in anisometropic amblyopia affect saccadic eye movements.

Methods:
Eighteen patients with anisometropic amblyopia and 18 control subjects participated. Participants executed saccades and manual reaching movements to a target presented randomly 5° or 10° to the left or right of fixation in 3 viewing conditions: binocular, amblyopic and fellow eye viewing. Latency, amplitude, and peak velocity of primary and corrective saccades were measured.

Results:
Initiation of primary saccades was delayed and more variable when patients viewed monocularly with their amblyopic eye. During binocular viewing, saccadic latency exhibited increased variability and no binocular advantage in patients (i.e., mean latency was similar to that during fellow eye viewing). The mean amplitude and peak velocity of primary saccades were comparable between patients and control subjects; however, patients exhibited greater variability in saccade amplitude. The frequency of corrective saccades was greater when patients viewed with their fellow eye in comparison to binocular or amblyopic eye viewing. Latency, amplitude and peak velocity of corrective saccades in patients were normal in all viewing conditions.

Conclusion:
Saccades had longer latency and decreased precision in amblyopia. Once saccades were initiated, however, the dynamics of saccades were not altered. These findings suggest that amblyopia is associated with slower visual processing in the afferent (sensory) pathway, rather than a deficit in the efferent (motor) pathway of the saccadic system.

References: None

Key Words: Oculomotor, Amblyopia, Binocular

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