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Hotel del Coronado • San Diego, California

PLATFORM SESSION II

Tuesday, February 24, 2015 • 7:30 a.m. - 12:00 p.m.

Moderators: Heather Moss, MD & Matthew Thurtell, MBBS, and FRACP – before break

Moderators: Rudrani Banik, MD & Timothy McCulley, MD - after break

- 7:30 a.m. - 7:45 a.m. Stacy L. Pineles
Improvements in Binocular Summation after Strabismus Surgery
- 7:45 a.m. - 8:00 a.m. Konrad P. Weber
A Novel Diagnostic Tool for Myasthenia Gravis: Ocular Vestibular Evoked Myogenic Potentials (Ovemp)
- 8:00 a.m. - 8:15 a.m. Joseph L. Demer
Compartmentalization of Superior Oblique (SO) Muscle Function has Implications for Superior Oblique Palsy
- 8:15 a.m. - 8:30 a.m. Agnes M. F. Wong
Development of Audiovisual Integration in Children and Adults with Amblyopia
- 8:30 a.m. - 8:45 a.m. Kevin R. Sitko
Pitfalls in the Use of Stereopsis for the Diagnosis of Non-Organic Visual Loss
- 8:45 a.m. - 9:00 a.m. Sui H. Wong
Natural History of Ocular Myasthenia Gravis in 101 cases: Towards a Risk of Generalization ('ROG') Score.
- 9:00 a.m. - 9:15 a.m. Joao Lemos
Cortical Control of Vertical Versus Horizontal Saccades in Parkinsonian Syndromes: An fMRI Study
- 9:15 a.m. – 9:30 a.m. Update: *The Journal of Neuro-Ophthalmology*
Lanning Kline, MD, Editor-in-Cheif
- 9:30 a.m. – 10:00 a.m. Coffee Break: Crown Room**
- 10:00 a.m. - 10:15 a.m. Y. Joyce Liao
Long Distance Homonymous Hemi-Macular Retrograde Degeneration of the Visual Pathway: A Comparison of Anterior and Posterior Visual Pathway Lesions
- 10:15 a.m. - 10:30 a.m. Christian A. Otto
Astronaut Preflight Cardiovascular Health is Highly Correlated with Postflight Eye Outcome Measures in the Visual Impairment Intracranial Pressure (VIIP) Risk Following Long Duration Spaceflight
- 10:30 a.m. - 10:45 a.m. Tiffany J. Hwang
Natural History of Conversion of Patients with LHON

- 10:45 a.m. - 11:00 a.m. Gary L. Yau
The Association of Intraocular Pressure on Visual Function in Papilledema from Idiopathic Intracranial Hypertension
- 11:00 a.m. - 11:15 a.m. Jaclyn J. Hwang
Dramatic Fixation Instability in Peripheral Vestibulopathies without Visual Feedback Compared with Central Vestibulopathies
- 11:15 a.m. - 11:30 a.m. Jorge C. Kattah
A Radiographic Target Sign for Abnormal Vertebral Artery Flow in Stroke Patients with Acute Vestibular Syndrome
- 11:30 a.m. - 11:45 a.m. Rachel C. Nolan
20/40 or Better Visual Acuity after Optic Neuritis: Not as Good as We Once Thought
- 11:45 a.m. - 12:00 p.m. Enrique J. Rivera
Chronic Optic Neuropathy Causes Decreases in both Inner Retinal Blood Flow and Prelaminar Optic Nerve Blood Flow

Tuesday, February 24, 7:30 - 7:45 a.m.

Improvements in Binocular Summation after Strabismus Surgery

Stacy L Pineles¹, Joseph L Demer¹, Sherwin J Isenberg¹, Eileen E Birch², Federico Velez¹

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Introduction:

Binocular summation (BiS), or improvement in vision using binocular vision compared to the better eye alone, is diminished in patients with strabismus. However, it is still not known how strabismus surgery affects BiS.

Methods:

Ninety-seven subjects recruited within one month before undergoing strabismus surgery underwent high and low contrast visual acuity testing binocularly and monocularly at pre-operative and two month post-operative visits. BiS was calculated for high contrast ETDRS and Sloan low contrast acuity (LCA) charts at 2.5% and 1.25% levels as the difference between the binocular score and that of the better eye. Pre-operative and post-operative values were compared.

Results:

There was a significant improvement in BiS at the two low contrast levels for all subjects, and for all contrast levels in the 75 patients in whom surgery successfully restored binocular alignment. For LCA, the proportion of subjects with BiS >5 letters post-operatively was almost twice that pre-operatively (16% to 30% and 11% to 21% for 2.5% and 1.25% contrast, respectively). Similarly, the proportion of subjects with binocular inhibition (binocular score worse by at least 5 letters than better eye score) was decreased post-operatively at all contrast levels (from 19% to 9% for 1.25% contrast). Twenty-eight percent of subjects experienced improvement in BiS scores post-operatively at the lowest contrast level.

Conclusions:

BiS scores improved post-operatively in most subjects undergoing strabismus surgery. This occurred most frequently at the lowest contrast level. Improved BiS represents a newly recognized functional benefit from surgical correction of strabismus, which is especially important in adults who were previously thought to achieve only psychosocial benefits.

References:

1. Pineles SL, Velez FG, Isenberg SJ, et al. Functional Burden of Strabismus: Decreased Binocular Summation and Binocular Inhibition. *JAMA Ophthalmol.* 2013;131(11):1413-1419.
2. Pineles SL, Birch EE, Talman LS, et al. One eye or two: a comparison of binocular and monocular low-contrast acuity testing in multiple sclerosis. *Am J Ophthalmol.* Jul 2011;152(1):133-140.
3. Tandon A, Velez FG, Isenberg SJ, Demer JL, Pineles SL. Binocular inhibition in strabismic patients is associated with diminished quality of life. *J AAPOS.* 2014;in press.

Keywords: Binocular Summation, Strabismus, Strabismus Surgery, Binocularity

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Tuesday, February 24, 7:45 - 8:00 a.m.

A Novel Diagnostic Tool for Myasthenia Gravis: Ocular Vestibular Evoked Myogenic Potentials (oVEMP)

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Introduction:

Diagnosis of myasthenia gravis (MG) can be challenging, especially in patients with isolated ocular involvement, negative autoantibodies and absence of the characteristic decrement in repetitive nerve stimulation. Ocular vestibular evoked myogenic potentials (oVEMP) are a recently developed, non-invasive test that allows electromyographic registration of extraocular muscle activity. Originally, the test was designed to assess vestibular function. We adapted oVEMP to detect the decrement in extraocular muscles of MG patients.

Methods:

26 MG patients and 17 healthy controls participated. We applied vibration stimuli to the forehead and recorded activity of the inferior oblique eye muscle with two surface electrodes placed beneath the eyes. To identify the oVEMP parameters with the highest sensitivity and specificity, we evaluated the decrement over 10 stimulus repetitions at three different repetition rates (3Hz, 10Hz, 20Hz).

Results:

Mean age of MG patients and controls was 57±18 and 40±17 years, respectively. Mean disease duration was 43±57 months. All MG patients had ocular symptoms, including ptosis (n=26) and diplopia (n=20). Twelve patients (46%) had isolated ocular symptoms, 4 (15%) had additional bulbar weakness and 10 (39%) generalized muscle weakness. Repetitive stimulation at 20Hz appeared to yield the best differentiation between MG patients and controls. Specifically, we found a bilateral decrement of >15% between the 2nd and 9th stimulus in 15 MG patients (58%) but in none of the controls (p<0.001). Among the 12 patients with isolated ocular MG, 11 (92%) showed a decrement (7 (58%) bilaterally, 4 (33%) unilaterally).

Conclusions:

Preliminary data of our study suggest that the presence of an oVEMP decrement is sensitive for MG, especially for its isolated ocular form. Thus, oVEMP should be considered a promising, additional diagnostic tool in MG. This simple, non-invasive test can be implemented in any neuromuscular clinic.

References: None.

Keywords: Myasthenia Gravis, Ocular Vestibular Evoked Myogenic Potentials (oVEMP), Electromyography, Eye Muscle, Decrement

Financial Disclosures: The authors had no disclosures.

Grant Support: Forschungskredit of the University of Zurich.

Tuesday, February 24, 8:00 - 8:15 a.m.

Compartmentalization of Superior Oblique (SO) Muscle Function Has Implications for Superior Oblique Palsy

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Introduction:

Intramuscular innervation of horizontal rectus extraocular muscles is divided into inferior and superior divisions innervating non-overlapping compartments of parallel-oriented muscle and tendon fibers. Functional magnetic resonance imaging (MRI) has demonstrated differential contractile function of horizontal rectus compartments during vertical duction, convergence, and ocular counter-rolling, as well as selective neurogenic atrophy in superior compartment lateral rectus palsy. We sought evidence of compartmental specialization in the SO, suspecting that selective damage to one or the other compartment might underlie some of the variation in clinical presentations of SO palsy.

Methods:

Gross dissections and 3-dimensional reconstructions of the intramuscular trochlear nerve were performed in humans, monkeys, cows, and rabbits. Multipositional, surface coil MRI was performed in 14 normal volunteers during 1° prism-induced vertical fusional vergence, and in central gaze in 19 patients with SO palsy, evaluating contractility by quantitative analysis of differential compartmental volume changes.

Results:

External to the SO belly, the trochlear nerve bifurcates into medial and lateral divisions innervating non-overlapping groups of muscle fibers. Gross dissection demonstrates that the inferolateral SO compartment inserts posteriorly on the sclera for mainly vertical action, while the superomedial portion inserts anteriorly for mainly torsional action. Traction on muscle fibers in one cadaveric compartment was transmitted selectively to the corresponding region of the scleral insertion. In normal volunteers, these compartments contracted differently during vertical fusional vergence. Eight of 19 patients with SO palsy exhibited elongated SO cross sections on MRI suggestive of neurogenic atrophy thinning only one compartment, and exhibited strabismus patterns differing from those with generalized SO atrophy.

Conclusions:

The SO functions as two parallel muscles specialized for vertical vs. torsional effects, and having separate peripheral innervation differentially susceptible to trochlear nerve pathology. Variable patterns of differential compartmental impairment contribute to the wide spectrum variations in patterns of cyclovertical incomitance in SO palsy.

References:

1. Demer. Compartmentalization of extraocular muscle function. Eye, (in press) 2014.
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Keywords: Superior Oblique Palsy, Extraocular Muscle, Hypertropia, Trochlear Nerve, Functional MRI of Extraocular Muscle

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH grant EY08313.

Tuesday, February 24, 8:15 - 8:30 a.m.

Development of Audiovisual Integration in Children and Adults with Amblyopia

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Introduction:

The McGurk effect is an audiovisual illusion that involves the concurrent presentation of a phoneme (auditory syllable) and an incongruent viseme (visual syllable). Adults with amblyopia show less susceptibility to this illusion than visually normal controls, suggesting a deficit in audiovisual integration. The present study investigated the developmental trajectory of audiovisual integration in both adults and children with amblyopia using the McGurk effect.

Methods:

Sixty-two participants with amblyopia (22 adults, 12 older children, 28 younger children) and 66 visually normal controls (25 adults, 17 older children, 24 younger children) viewed videos that combined phonemes and visemes, and were asked to report what they heard. Videos with both congruent (auditory and visual matching) and incongruent (auditory and visual not matching) stimuli were presented. Incorrect responses on incongruent trials correspond to a strong McGurk effect, indicating that the viseme influenced the phoneme (i.e., strong audiovisual integration).

Results:

Participants with amblyopia demonstrated a weaker McGurk effect than visually normal controls across all age groups. Effect strength increased with age for both amblyopic participants and controls. Both groups showed a similar response pattern to different speakers and syllables, but amblyopic participants consistently demonstrated a weaker effect.

Conclusions:

Amblyopia is associated with deficits in audiovisual integration in both children and adults. Our findings indicate that the deficits are not simply a delay in development of audiovisual integration in children with amblyopia; rather they represent permanent deficits that persist into adulthood.

References: None.

Keywords: Pediatric Neuro-Ophthalmology, Multisensory Integration, Amblyopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Tuesday, February 24, 8:30 - 8:45 a.m.

Pitfalls in the Use of Stereopsis For the Diagnosis of Non-Organic Visual Loss

Kevin R. Sitko¹, Jason H. Peragallo^{1,5}, Samuel S. Bidot¹, Valerie Biousse^{1,2}, Nancy J. Newman^{1,2,3}, Beau B. Bruce^{1,2,4}

Introduction:

Polarized vectogram stereoacuity testing is used to estimate visual acuity (VA) in the diagnosis of non-organic visual loss (NOVL),¹ but only predicts mean VA and doesn't account for normal inter-subject variability. These predictions were derived from optical degradation of VA in normal subjects and may not account for the variability seen in patients with neuro-ophthalmic pathologies included in the differential diagnosis of NOVL.^{2,3}

Methods:

All patients presenting to our service between 4/25/2014 and 6/26/2014 underwent routine neuro-ophthalmic examination, including polarized vectogram stereoacuity measurements (Titmus). A compound Bayesian logit-lognormal model accounting for heteroskedasticity was used to determine 95% and 99% prediction intervals of the worse eye's near visual acuity (VA) based on stereoacuity. LogMAR acuity and log stereoacuity were analyzed.

Results:

Of 405 patients, 16 were excluded for missing stereoacuity or VA measurements, 3 for cognitive issues, 3 for suspected NOVL, and 92 for heterotropia or history of strabismus/amblyopia. Patients who correctly identified zero circles (34) were also excluded from the calculation. 257 subjects were analyzed [median age: 45-yo (range: 11-91); 184(72%) women; median worse-eye VA 20/25; median: 7 circles correct]. Stereoacuity was positively associated with VA: 9 circles correct (40 seconds of arc) indicated VA of at least 20/39 with 95% confidence and 20/79 with 99% confidence; 6 circles correct (80 seconds of arc): 20/61 and 20/178; and 4 circles correct (140 seconds of arc): 20/103 and 20/544, respectively.

Conclusions:

When fully accounting for individual variation and the full spectrum of neuro-ophthalmic diseases affecting VA, stereoacuity remains associated with VA, but commonly-used VA estimates based on stereoacuity overestimate VA. Our results more accurately predict minimum VA from polarized vectogram stereoacuity and should be preferentially used when evaluating patients with suspected non-organic visual loss. We demonstrate that polarized vectogram stereoacuity cannot establish definitively normal VA, and therefore can only suggest, but not establish, the diagnosis of NOVL.

References:

1. Miller NR, Newman NJ, Biousse V, and Kerrison JB, eds. Walsh & Hoyt's Clinical Neuro-Ophthalmology, 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2005, vol. 1
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Keywords: Stereopsis, Non-organic, polarized stereogram, vectogram

Tuesday, February 24, 8:45 - 9:00 a.m.

Natural History of Ocular Myasthenia Gravis in 101 cases: Towards a Risk of Generalization ('ROG') Score.

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Introduction:

There is currently no prognostic test to individualize prediction of Generalized Myasthenia Gravis (GMG) risk in patients who first present with ocular disease. Most studies that report risk factors are flawed by the mix of patients on immunosuppression. We aimed to create a prognostic score to predict the risk of GMG.

Methods:

Multi-centre retrospective cohort study of patients with OMG for minimum 3months, untreated with immunosuppression for minimum 2years or until GMG onset. Data analyzed by logistic regression to develop the predictive score for GMG at 2years.

Results:

101(57F) patients were included, with mean follow-up 8.4y(2-42) from disease onset. 31 developed GMG at median 1.31y(3.5mo-20.2y); 19 occurred within 2years. Univariable logistic regression analysis produced three significant predictors($p < 0.10$); adjusted ORs in a multivariable logistic model (Chi-square $p = 0.001$): seropositivity 5.63(95%CI,1.42-22.33); presence of one or more comorbidity 5.56(95%CI,0.66-46.62); thymic hyperplasia 6.66(95%CI,0.45-98.01). Prognostic score derived from the coefficients of the logistic model: sum of the points (one point for presence of each of the above predictive factors); classified 'low risk' if ≤ 1 , 'high risk' if ≥ 2 . Predicted probabilities: 0.07(SD 0.03) for 'low risk', 0.39(SD 0.09) for 'high risk'. Negative predictive value(NPV) 91%(95%CI,79-98), Positive Predictive Value 38%(95%CI,23-54), Sensitivity 79%(95%CI,54-94), Specificity 63%(95%CI,50-74), area under Receiver Operating Characteristic curve 0.74(95%CI,0.64-0.85).

Conclusions:

We present one of the few natural history studies on OMG and describe risk factors for GMG not previously reported (thymic hyperplasia, presence of comorbidities), but do not show association with others (age, sex, autoimmunity). We created the first predictive score to prognosticate the risk of GMG. The high NPV is useful in identifying low risk patients, and can complement decision-making and counsel patients at diagnosis. This approach of risk stratification moves us towards addressing the question of modifying GMG risk in high-risk patients. Furthermore the effect of comorbidities is novel and demands further elucidation.

References: None.

Keywords: Myasthenia Gravis, Ocular Myasthenia Gravis, Prognosis

Financial Disclosures: The authors had no disclosures.

Grant Support: None

Tuesday, February 24, 9:00 - 9:15 a.m.

Cortical Control of Vertical Versus Horizontal Saccades in Parkinsonian Syndromes: An fMRI study

João Lemos¹, Daniela Pereira^{2,3}, Luciano Almendra¹, Diliãna Rebelo³, João Castelhana³, Gil Cunha^{2,3}, Cristina Januario^{1,4}, Luis Cunha^{1,4}, Antonio F Goncalves^{1,4}, Miguel Castelo-Branco^{3,4}

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Introduction:

Examination of saccades has gained overwhelming acceptance as a clinical tool in evaluation of parkinsonian syndromes. While Parkinson's disease patients usually evidence hypometric self-paced saccades, patients with progressive supranuclear palsy characteristically show small and slow saccades, especially in the vertical direction. Although the brainstem structures responsible for the control of saccades have been thoroughly studied, the cortical saccadic circuitry, particularly for vertical saccades is far less known. We sought to compare functional Magnetic Resonance Imaging (fMRI) activation between two parkinsonian syndromes during the execution of vertical and horizontal saccades.

Methods:

In this ongoing study, we measured perisaccadic blood oxygenation-level dependent (BOLD) activation in Parkinson's disease (PD) patients (n=19), progressive supranuclear palsy (PSP) patients (n=4) and controls (CTs; n=17) while performing a block-design task, consisting of two runs (prosaccades, PS; antisaccades, AS) of 6 blocks each (3 vertical, V; 3 horizontal, H).

Results:

In V>H (PS) within groups effects analysis, CTs showed no significant differences between vertical and horizontal prosaccades. In contrast, PD and PSP patients showed greater activations, particularly in the latter group: left intraparietal sulcus (IPS) in PD patients and left dorsolateral prefrontal cortex and anterior and posterior cingulate gyrus in PSP patients. Regarding V>H (AS) within groups effects analysis, an opposite phenomenon was noted across groups, again particularly marked in PSP patients: several hypoactivations were found, including in bilateral occipital cortex in CTs, left ventral striatum in PD patients, and bilateral orbitofrontal cortex, ventral striatum, thalamus and left fusiform gyrus in PSP patients.

Conclusions:

Greater cortical activations during vertical prosaccades in parkinsonian patients may reflect a compensatory mechanism in an attempt to overcome specific saccadic deficits in these syndromes. Marked hypoactivations during vertical antisaccades in progressive supranuclear palsy patients possibly indicate additional cortical and sub-cortical impairment in response to a cognitively demanding task such as antisaccades, especially in the vertical direction.

References:

1. Amtage F, Maurer C, Hellwig S, Tüscher O, Kreft A, et al. Functional correlates of vertical gaze palsy and other ocular motor deficits in PSP: an FDG-PET study. *Parkinsonism Relat Disord*. 2014 Aug;20(8):898-906.
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Keywords: Ocular Motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: A grant from Portuguese Brain Imaging Network supported this study.

Tuesday, February 24, 10:00 - 10:15 a.m.

Long Distance Homonymous Hemi-Macular Retrograde Degeneration of the Visual Pathway: A Comparison of Anterior and Posterior Visual Pathway Lesions

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Introduction:

Trans-synaptic degeneration of the visual pathway following ablation of the striate cortex is well established in non-human primates and involves parvocellular retino-geniculate connections.¹⁻³ In humans, trans-synaptic degeneration is more controversial but has been described recently.⁴⁻⁹ In this study, we used optical coherence tomography (OCT) to examine the severity and timing of retrograde degeneration in human anterior (optic tract, lateral geniculate nucleus) and posterior (occipital) visual pathway lesions.

Methods:

We performed retrospective chart review of over 70 patients with homonymous visual field loss with confirmed lesions of the visual pathways on brain imaging studies. We analyzed the high quality OCT studies and correlated the findings with visual field loss and MRI. Statistical significance was determined using Mann-Whitney U test.

Results:

There was significant homonymous, hemi-macular thinning of the ganglion cell complex (ganglion cell layer + inner plexiform layer) in patients with anterior (N = 11, P = 0.0001) and posterior (N = 19, P = 0.006) visual pathway lesions, and the pattern of thinning correlated with that of visual field loss. Anterior lesions led to rapid, severe hemi-macular thinning within months (P < 0.0001), while posterior lesions were associated with relatively more modest and much slower thinning over years (anterior: 54.9 ± 2.3 µm, N = 11; posterior: 64.0 ± 2.5 µm; N = 18: P < 0.02). Within one-year, many cases of occipital lesions showed no thinning, even when the lesion was large. OCT studies performed 1-3 years after onset revealed progressive thinning over time. Patients with congenital or incidentally noted homonymous hemifield defects often exhibited hemi-macular thinning, presumably because the thinning has had years to develop.

Conclusions:

Retrograde, homonymous, hemi-macular thinning occurred in the human visual pathway over long distance, even trans-synaptically. There was more rapid and more severe thinning in anterior visual pathway lesions (optic tract, LGN) compared with that of occipital lobe lesions.

References:

1. Vanburen JM (1963) Trans-Synaptic Retrograde Degeneration in the Visual System of Primates. *J Neurol Neurosurg Psychiatry* 26:402-409.
2. Horoupian DS, Ghetti B, Wisniewski HM (1973) Retrograde transneuronal degeneration of optic fibers and their terminals in lateral geniculate nucleus of rhesus monkey. *Brain research* 49:257-275.
3. Weller RE, Kaas JH, Ward J (1981) Preservation of retinal ganglion cells and normal patterns of retinogeniculate projections in prosimian primates with long-term ablations of striate cortex. *Invest Ophthalmol Vis Sci* 20:139-148.
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Keywords: Trans-Synaptic Degeneration, Hemi-Macular Thinning, Visual Fields, Optical Coherence Tomography, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: Burroughs Wellcome Foundation Career Award in Biomedical Studies

Tuesday, February 24, 10:15 - 10:30 a.m.

Astronaut Preflight Cardiovascular Health is Highly Correlated with Postflight Eye Outcome Measures in the Visual Impairment Intracranial Pressure (VIIP) Risk following Long Duration Spaceflight

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Introduction:

Seventy percent of tested ISS astronauts demonstrate changes in ocular structure and function; 32% with disc edema, and five with elevated CSF pressure. Increased vascular compliance may predispose astronauts to VIIP. The purpose of this study was to determine if astronauts with higher preflight cardiovascular risk profiles demonstrated worse post flight eye outcomes.

Methods:

A preflight "cardiovascular profile" for 31 ISS astronauts was compiled using twelve parameters: systolic blood pressure, pulse pressure, body mass index, percentage fat, LDL, HDL, triglycerides, anti-lipid medication use, fasting glucose, maximal oxygen uptake, age, and salt intake. This profile was compared with seven postflight eye outcome variables: globe axial length; optic nerve sheath diameter, optic nerve diameter, optic nerve to sheath ratio, intraocular pressure, change in manifest refraction, and circumpapillary retinal nerve fiber layer. Twenty-two percent of the eye outcome data were missing; consequently, a multivariate multiple imputation technique with predictive mean matching methods was employed. Rubin's rules for collapsing the statistical results across the multiply imputed data sets was applied to assess the canonical correlation.

Results:

A highly significant canonical correlation of .97 ($p < .00001$) indicated a strong association between preflight cardiovascular health and postflight eye outcomes. The "joint test" revealed a significant difference in cardiovascular profile between male and female astronauts ($\text{Prob} > F = 0.00001$); female astronauts demonstrating a healthier cardiovascular profile.

Conclusions:

The presence of multiple cardiovascular risk factors is a known independent predictor of decreased vascular compliance¹. Preflight cardiovascular profile was strongly associated with VIIP eye outcome. Female astronauts had a significantly healthier cardiovascular profile than the males. No female astronaut has developed optic disc edema. We speculate that astronauts with poorer cardiovascular health have decreased vascular compliance resulting in: a higher 24 hour mean central venous pressure, cerebral venous congestion, decreased CSF resorption, and elevated ICP in space.

References:

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Keywords: Visual Impairment, Vascular Compliance, Intracranial Pressure, Spaceflight

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Tuesday, February 24, 10:30 - 10:45 a.m.

Natural History of Conversion of Patients with LHON

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Introduction:

Leber Hereditary Optic Neuropathy (LHON) is a maternally inherited disorder that presents as subacute asynchronous bilateral loss of vision in young adult males. While fundus changes have been described around time of conversion, no published studies include changes preceding conversion, as based on standard clinical criteria. We report the natural history of conversion of 6 patients whose funduscopy and clinical changes were recorded for more than 1 year pre- and post- conversion.

Methods:

A retrospective database initiated in 2001 of a 336 member seven-generation pedigree of 11778 mtDNA mutation, homoplasmic J-haplogroup LHON was reviewed for carriers who converted to affected status, resulting in twelve eyes from 6 patients included in this study. Medical records were reviewed 1 year pre- and post- conversion for: mean deviation, -logMAR, and RNFL thickness. Data from all 12 eyes were sorted, averaged, and analyzed within 2 month time periods.

Results:

Decrease in mean deviation occurred as early as 2 – 4 months preceding the date of conversion, after which values dropped precipitously until plateau at a complete loss of vision around 6 – 8 months. Decreased visual acuity as demonstrated by -logMAR was noted up to 2 months preceding the date of conversion, after which values continued to decrease at a fairly constant rate. Average RNFL thickness began increasing immediately at conversion, followed by a sharp decrease around 2 months post-conversion with a steady decline to plateau around 8 – 10 months.

Conclusions:

Early funduscopy changes in mean deviation suggest that structural changes precede functional conversion in LHON patients by up to 8 months. In addition, sub-clinical losses of vision were noted to precede the clinical date of conversion. RNFL changes support the suggested pathophysiology of initial RNFL swelling at conversion followed by dramatic atrophy. The criteria for establishing the date of conversion has not yet been objectively defined.

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Keywords: Optic Neuropathy, Diagnostic Tests, Genetic Disease, RNFL, OCT

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Tuesday, February 24, 10:45 - 11:00 a.m.

The Association of Intraocular Pressure on Visual Function in Papilledema from Idiopathic Intracranial Hypertension

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Introduction:

Idiopathic intracranial hypertension (IIH) frequently manifests as papilledema associated with visual loss. Recent studies suggest that higher intraocular pressure (IOP) may counteract the effect of elevated intracranial pressure (ICP) at the level of the lamina cribosa, possibly mitigating the damage to axonal transport and subsequent visual function. The current study aimed to test the hypothesis that eyes with higher IOP are associated with superior visual function in those with papilledema secondary to IIH.

Methods:

A retrospective, cross-sectional, paired-eye, comparison study was conducted on a consecutive series of newly diagnosed patients with IIH from a single Neuro-ophthalmology specialist practice between January 2006 and January 2014. Included subjects had baseline bilateral IOP measurements obtained by applanation tonometry and concurrent automated perimetry. Patients were divided into two groups for analysis. The first group had symmetric IOPs bilaterally (within 1 mmHg) whereas the second group had asymmetric IOPs (of 2 mmHg or greater) between eyes. The primary outcome was Mean Deviation (MD) as measured by perimetry.

Results:

Forty-four patients were analyzed, with 31 in the symmetric group and 13 in the asymmetric group. Baseline demographic characteristics were similar between both groups. When comparing MD between eyes, there was no difference in the symmetric group ($p = 0.89$), whereas a significant difference was observed in the asymmetric group ($p = 0.007$). Specifically, in the asymmetric group, the eye with the higher IOP (mean, 15.77 SD 2.52 mmHg) had less visual loss (MD: -5.72 SD 7.13 dB) compared to their fellow eye (MD: -7.04 SD 7.66 dB) with lower IOP (mean, 12.77 SD 2.92 mmHg).

Conclusions:

Patients presenting with papilledema from IIH with asymmetric IOP's display better visual function in the eye with higher IOP. This novel observation suggests that IOP may play an important role in visual loss from IIH. Further investigation into this relationship is warranted.

References: None.

Keywords: Pseudotumor Cerebri, High intracranial Pressure/Headache

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Tuesday, February 24, 11:00 - 11:15 a.m.

Dramatic Fixation Instability in Peripheral Vestibulopathies without Visual Feedback Compared with Central Vestibulopathies

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Introduction:

Eye movement abnormalities are common in central and peripheral vestibulopathies, and characterization of eye movements using infrared oculography can help teach us important ways to localize the lesion. In this study, we compare and contrast eye movement findings of patients with peripheral vestibulopathies with that of central pathway lesions.

Methods:

We performed 60-Hz 3D infrared oculography with and without a fixation target and analyzed fixation instabilities and waveform characteristics in 10 patients with peripheral and 10 patients with central vestibulopathies. Fixation target at distance in the light is displayed by a custom-made LED board. Fixation target in the dark is seen within the infrared recording goggle and turned on and off to assess changes in eye position. All patients had relatively mild or no dizziness at the time of recording.

Results:

In patients with peripheral vestibulopathies, such as acoustic neuromas or vestibular neuronitis, visual fixation at a distant target is typically good when the patient is relatively asymptomatic, with rare, small amplitude square wave jerks. Without visual feedback, patients can rapidly decompensate, exhibiting rapid deviations of eye positions, often in square wave jerk waveform with rapid on and off set and may be accompanied by a torsional nystagmus. In contrast, patients with central vestibular pathway lesions, such as Wallenberg syndrome or brainstem cavernous malformations, typically exhibit uni- or multi-directional oscillations initiated by a slow phase. Without visual feedback, patients with central vestibulopathies have less prominent changes in eye movement waveform.

Conclusions:

A useful test to distinguish peripheral and central vestibulopathies is to observe patient eye movement behavior during fixation with and without visual feedback, since peripheral vestibular patients are more likely to exhibit dramatic and rapid fixation instability without visual feedback.

References: None.

Keywords: Nystagmus, Eye Movement Abnormality, Peripheral Vestibulopathy, Central Vestibulopathy, Dizziness

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Tuesday, February 24, 11:15 - 11:30 a.m.

A Radiographic Target Sign for Abnormal Vertebral Artery Flow in Stroke Patients with Acute Vestibular Syndrome

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Introduction:

Stroke involving the brainstem and cerebellum may present with isolated acute vestibular syndrome (AVS). Vertebral artery (VA) thrombo-embolism or dissection is a potential cause, and may be noted as a VA flow abnormality seen as V4 segment hyper-intensity or asymmetry on axial T2 MRI.

Methods:

Retrospective study of 223 AVS patients presenting over 15 years to a single stroke referral center. Of these, 145 had available T2 MRI scan (160 scans). Axial T2 MRIs were reviewed by a blinded neuro-radiologist and a non-blinded clinician for presence of V4 segment hyper-intensity or asymmetry (target sign). Disagreements were adjudicated. We report percentages for presence of target sign in each group, odds ratio, target sign and lesion laterality, presence of target sign in stroke patients with negative initial DWI MRI, and Kappa for inter-rater reliability.

Results:

Of the 145 AVS patients with available axial T2 MRI scans, 71 had stroke, and 74 were diagnosed with vestibular neuritis (VN). VA V4 segment hyper-intensity was seen in 42.2% of stroke patients (30/71), and 8.1% of patients with VN (6/74). Odds ratio of stroke in patients with a "target sign" was 8.29 (95% CI 3.18-21.6). With the exception of one stroke patient, all found target signs were ipsilateral to the side of final stroke. Among stroke patients with negative initial DWI MRI, 41.7 % (5/12) had a VA V4 segment hyper-intensity. Cohen's kappa for inter-rater reliability was 0.78.

Conclusions:

The VA V4 segment hyper-intensity or "target sign" identified pathologic VA abnormalities in a nearly half of stroke patients presenting with AVS. In VN, the target sign was uncommon. The VA target sign may precede restricted diffusion, and may help distinguish stroke from VN in selected acute presentations. When present, it should prompt clinicians to repeat DWI MRI to confirm a potentially missed ischemic cerebrovascular syndrome.

References: None.

Keywords: Vertigo, Vestibular Neuritis, Stroke, Vertebral Artery Stenosis, Neuroimaging

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20/40 or Better Visual Acuity After Optic Neuritis: Not as Good as We Once Thought

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Introduction:

It has been reported that patients with acute optic neuritis (ON) have good visual recovery, with return of high-contrast visual acuity (VA) to 20/40 or better in 95% of affected eyes. Vision-specific quality of life (QOL), however, is reduced among overall cohorts of patients with history of ON, even years following the acute event. We examined vision-specific QOL scores in a cohort of multiple sclerosis (MS) patients among the specific sub-group of subjects with history of ON and high-contrast VA of 20/40 or better in both eyes.

Methods:

Participants in an ongoing collaborative study of MS visual outcomes completed 25-Item National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25) and 10-Item Neuro-Ophthalmic Supplement, as well as VA and low-contrast letter acuity (LCLA) testing. Spectral-domain optical coherence tomography (SD-OCT) was performed to determine peripapillary retinal nerve fiber layer thickness (RNFL) and macular ganglion cell+inner plexiform layer thickness (GCL+IPL).

Results:

Analyses of data from 247 patients with MS (age 47.1±11.6 years) showed that among those with a history of ON (n=128), vision-specific QOL scores were reduced compared to disease-free controls even among the sub-group with VA 20/40 or better in both eyes (n=106, p<0.001 for NEI-VFQ-25 composite and 10-Item Supplement, linear regression, accounting for age). Specifically, NEI-VFQ-25 scores were 83.6±14.7 (compared to 98.4±1.8 for controls), with Supplement scores 73.8±17.9 (vs. 96.8±4.9 for controls). Those with greater binocular LCLA had better QOL scores (2.5%: p=0.02; 1.25%: p=0.006, accounting for age). Eyes in this sub-group had significant thinning of the RNFL (79.8 vs. 93.0 microns for controls, p<0.001) and GCL+IPL (69.7 vs. 80.4 microns, p<0.001, accounting for age and within-patient, inter-eye correlations).

Conclusions:

Even when VA is 20/40 or better, patients with history of acute ON are left with clinically meaningful reductions in vision-specific QOL, and manifest significant degrees of retinal axonal and neuronal loss.

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Keywords: Optic Neuritis, Quality of Life, Multiple Sclerosis, Binocular Vision, Optical Coherence Tomography

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Chronic Optic Neuropathy Causes Decreases in Both Inner Retinal Blood Flow and Prelaminar Optic Nerve Blood Flow

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Introduction:

Our purpose was to determine if optic neuropathy results in an obligatory decrease in blood flow to the inner retina and optic nerve due to decreased metabolic demand from non-functioning neurons. Visual stimulation causes transient hyperemia, but it is unknown if decreases in neuron activity cause reduced blood flow.

Methods:

Laser speckle blood flowgraphy imaging (LSFG-NAVI; Softcare Ltd, Fukuoka, Japan) was performed on a 25x20 degree area of the fundus incorporating the optic nerve head. Blurring of the laser speckle pattern by moving particles in the image plane was used to simultaneously measure blood flow in the major circumpapillary retinal arteries and veins, and below the surface of the optic nerve head. Blood flow was determined in each eye of 19 patients with unilateral optic neuropathy (ischemic=13, compressive=5, inflammatory=1) in the chronic state. Inner retinal blood flow and optic nerve head blood flow were compared between affected and unaffected eyes. Retinal nerve fiber layer (RNFL) and retinal ganglion cell layer complex (GCL) were compared to retinal and optic nerve blood flow.

Results:

There was a significant decrease in inner retinal blood flow in eyes with optic neuropathy compared to the fellow normal eye ($P=0.002$; mean= $69\pm 17\%$ of fellow eye). A significant decrease in optic nerve head blood flow deep to the superficial retinal capillaries was also present ($P<0.001$; mean= $65\pm 22\%$ of fellow eye). There was also significant decrease in both RNFL ($P=0.02$; mean= $83\pm 32\%$ of fellow eye) and GCL thickness ($P<0.001$; mean= $71\pm 11\%$ of fellow eye), but no significant correlation between the inter-ocular asymmetry of retinal or optic nerve blood flow and RNFL or GCL thickness.

Conclusions:

Chronic optic neuropathy results in decreased retinal and optic nerve head blood flow, likely due to reduced metabolic demand. Laser speckle blood flowgraphy allows non-invasive simultaneous measurement of retinal, choroidal, and optic nerve head blood flow.

References: None.

Keywords: Optic Neuropathy, Vascular Disorders, Diagnostic Tests

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