Platform Session II

Arizona Salons 1-6

Tuesday, March 9, 2010

7:30 a.m. – 12:00 p.m.

Moderators: Agnes Wong, MD, PhD, FRCS(C) and Prem Subramanian, MD, PhD – before break

Moderators: Alfredo Sadun, MD, PhD and Michael Lee, MD – after break

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7:30 a.m. - 7:45 a.m.

Growth Factors Enhance Differentiation of Adult Bone Marrow Derived Stem Cells in Ischemic Murine Retina

Nitza Goldenberg-Cohen[2], Bat-Chen R. Avraham-Lubin[1], Nadir Askenasy[3]

[1]The Krieger Eye Research Laboratory, FMRC, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, [2]Ophthalmology Department, Pediatric Unit, Schneider Children's Medical Center of Israel, Petah Tikva, Israel, [3]Frankel Laboratory for Stem Cell Research, Pediatric Hemato-Oncology department, Schneider Children's Medical Center of Israel, Petah Tikva, Israel

Introduction:
Candidate stem cells of neuronal, retinal and embryonic origin have been shown to incorporate differentially in the retina in various injury models. We used a model of acute ischemic optic neuropathy (rAION) to evaluate the potential of candidate adult bone marrow-derived stem cells (aBMSC) to reconstitute injured retina. We have previously observed efficient incorporation of putative aBMSC in the retina following rAION. In this study we assessed the possibility to direct the differentiation of the cells by local intravitreal administration of brain derived neurotrophic factor (BDNF) ciliary neurotrophic factor (CNTF) and vascular endothelial growth factor (VEGF).

Methods:
Injury was induced by photoactivation of Rose Bengal over the optic disk, causing predominant death in the retinal ganglion cell (RGC) layer. The smallest subset of nucleated bone marrow cells were collected by counterflow centrifugal elutriation and depleted of cells expressing lineage markers (Fr25Lin-aBMSC). The candidate SC were injected intravitreouslly or intravenously. Subsequently, BDNF, CNTF or VEGF were directly administered into the vitreous body.

Results:
Few cells incorporated into the injured retina in the absence of growth factors, and displayed various differentiation markers as determined by co-localization of donor markers (GFP and Y chromosome). In the BDNF-, CNTF- and VEGF-treated eyes, GFP+ aBMSC incorporated preferentially in the RGC layer and displayed neuronal markers. Few retina-engrafted cells were GFAP-positive astrocytes, as determined from location, shape and markers. Donor cells incorporation in the VEGF-injected group mainly expressed glial and endothelial markers.

Conclusion:
Microenvironmental alterations caused by acute ischemic injury of the optic nerve and retina facilitate homing and incorporation of stem cells. Intravitreal injection of growth factors increased the efficacy of donor cell incorporation and enhanced glial differentiation. These data demonstrate that aBMSC participate in retinal regeneration through neogenesis of glia and endothelium, and express neuronal markers as a feature of developmental plasticity.

References: NONE

Key Words: adult bone marrow derived stem cells, ischemic optic neuropathy, mouse model, growth factor, enhanced differentiation

Financial Disclosure: NONE

7:45 a.m. - 8:00 a.m.

Prevalence of Smooth Pursuit and Reflexive Saccades Abnormalities in Congenital Ocular Motor 'Apraxia'

Michael Salman

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Introduction:
Congenital ocular motor apraxia (COMA) refers to a defect in initiating saccades on command. It is a sign and not a distinct disease entity. COMA is commonly associated with developmental delay. The pathogenesis of COMA is unknown but a recent proposal suggested that bilateral damage or disconnection between left and right ocular motor regions involved in processing saccades may be responsible for COMA.[1] Since saccades and smooth pursuit (SP) are processed by several common brain regions such as the frontal eye field and the cerebellum, the author hypothesized that the prevalence of SP impairment in COMA is high. In addition, the prevalence of deficits in reflexive saccade (RS) in COMA was investigated to ascertain the suitability of the term 'apraxia' in describing this clinical sign.

Methods:
Twenty seven studies describing SP and/or RS in 211 patients, 9 weeks to 38 years old, with COMA were analyzed. Information was available on: 1) SP in 122 (19 studies), 2) the fast phases of the vestibulo-ocular reflex in 129 (15 studies), and 3) the optokinetic response in 194 patients (23 studies).

Results:
SP impairment was reported in 95 patients (78%) with COMA including at least (25/41) 61% of patients who did not have Joubert syndrome. Deficits in the fast phases of the vestibulo-ocular reflex and optokinetic response were reported in 126 (97.7%) and 186 (95.9%) patients respectively. Most patients had developmental delay.

Conclusion:
Smooth pursuit impairment occurs frequently in COMA, even in patients who do not have Joubert syndrome where SP impairment commonly occurs. This suggests that COMA is not just a disorder of saccadic initiation. The high prevalence of development delay in these patients is consistent with more widespread brain dysfunction. The use of the term 'apraxia' is not suitable since most patients had reflexive saccades deficits in addition to deficits in initiating voluntary saccades.

References:
1. Salman MS, Ikeda KM, Wrogemann J. Ocular motor apraxia: Disconnections and compensations, Can J Neurol Sci, 36(3, Suppl 1), S57, 2009 (Abstract)

Key Words: Ocular motor, saccades, smooth pursuit, Ocular motor apraxia,

Financial Disclosure: NONE

8:00 a.m. - 8:15 a.m.

Juvenile Ocular Myasthenia Gravis: Risk of Generalization and Amblyopia

Heather Moss, Stacy Pineles, Grant Liu

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Introduction:
There have been only a few studies evaluating visual and systemic outcomes, such as amblyopia or systemic generalization, in pediatric ocular myasthenia gravis (OMG).[1-4] Furthermore, treatment regimens and outcomes in these studies were varied, and there has been no conclusion on whether more aggressive treatments help prevent undesirable outcomes.

Methods:
The charts of all pediatric patients (aged 1-18 years) diagnosed with OMG based upon published criteria[5], and with minimum follow-up of 1 year were retrospectively reviewed. Data recorded included age, visual acuity, motility, presence of ptosis or strabismus, treatment, time to resolution or generalization, and amblyopia. In addition, we compared our treatment regimen and results with those reported previously.

Results:
Thirty-nine patients were identified, with a mean age of 5.4±4.8 years and mean follow-up of 5.2±4.3 years. Fifteen patients were treated with pyridostigmine only, 19 (49%) also received steroids, and 16 (41%) underwent thymectomy or steroid-sparing immunosuppressive therapy. When compared with the majority of prior studies[1-4], our patients were more commonly treated with steroids or thymectomy. There was no correlation between sex or age with amblyopia or generalization. Resolution occurred in 10 patients, and generalization in six. Although 9 patients were treated for amblyopia, only 2 had amblyopia at the final visit.

Conclusion:
In our series, 26% of patients had resolution of symptoms, and 18% had systemic generalization. Amblyopia occurred in 24% of patients, but was only present at the final visit in 5%. Our larger cohort confirms previous findings that juvenile OMG has a relatively low risk of generalization in treated patients, and that related amblyopia is readily treatable. Although our treatments appeared more aggressive than those previously reported, our rates of amblyopia and systemic generalization are comparable, and therefore suggest that 2nd and 3rd line therapies do not necessarily improve overall outcomes in pediatric OMG.

References:
1. Ortiz, S, and Borchert, M. Long-term outcomes in pediatric ocular myasthenia gravis. Ophthalmology 2008; 115:1245-8l.
2. Kim, JH, Hwang, JM, Hwang, YS, Kim, KJ, Chae, J. Childhood ocular myasthenia gravis. Ophthalmology 2001; 110:1458-62.
3. Mullaney, P, Vajsar, J, Smith, R, Buncic, JR. The natural history and ophthalmic involvement in childhood myasthenia gravis at The Hospital for Sick Children. Ophthalmology 2000; 107:504-10.
4. McCreery, KM, Hussein, MA, Lee, AG, Paysse, EA, Chandran, R, Coats, DK. Major review: the clinical spectrum of pediatric myasthenia gravis: blepharoptosis, ophthalmoplegia and strabismus: a report of 14 cases. Binocul Vis Strabismus Q; 17:181-6.
5. Kupersmith, MJ. Does early immunotherapy reduce the conversion of ocular myasthenia gravis to generalized myasthenia gravis? J Neuro-Ophthalmol 2003; 23: 249-50.

Key Words: myasthenia gravis, amblyopia

Financial Disclosure: NONE

8:15 a.m. - 8:30 a.m.

Multi-System Neurological Disease Is Common In Patients with *OPA1* Mutations

Patrick Yu-Wai-Man[1], Philip G. Griffiths[2], Grainne S. Gorman[1], Charles M. Lourenco[3], Alan F. Wright[4], Michaela Auer-Grumbach[5], Guy Lenaers[6], Douglass M. Turnbull[1], Marcela Votruba[7], Massimo Zeviani[8], Valerio Carelli[9], Lawrence Bindoff[10], Rita Horvath[11], Patrizia Amati-Bonneau[12], Patrick F. Chinnery[1]

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Introduction:
Autosomal dominant optic atrophy (DOA) classically presents in early childhood with progressive visual failure, and about 60% of families harbor pathogenic mutations in the *OPA1* gene (3q28-q29).[1,2] However, *OPA1*+ve families have recently been described where the visual loss also segregated with more severe neuromuscular deficits, so-called "DOA+" variant.[3,4] Given that only 7 families were reported, the broader clinical significance of these observations was unclear. We therefore conducted a systematic clinical and molecular study of *OPA1*+ve families to establish the frequency of DOA+ in *OPA1* disease and to describe the natural history of these additional neuromuscular features.

Methods:
OPA1 +ve families included in this study were assembled as part of a prospective epidemiological survey of inherited optic neuropathies in the North of England, with contributions from other diagnostic and research centres with an interest in mitochondrial genetic disorders.

Results:
Multi-system neurological disease developed in 17.2% of all *OPA1* mutational carriers and this was associated with significantly worse visual outcomes. Based upon a meta-analysis of 104 patients from 49 independent DOA+ families, bilateral sensorineural deafness was the most prominent manifestation (66.3%), followed by a combination of ataxia, myopathy, neuropathy and chronic progressive external ophthalmoplegia. We also further expand the phenotypic spectrum of *OPA1* disease with previously unreported clinical manifestations as spastic paraplegia and a multiple sclerosis-like illness. DOA+ was associated with all *OPA1* mutational subtypes, although there was a two to three-fold increased risk with missense mutations located within the catalytic GTPase domain. Skeletal muscle biopsies showed unequivocal features of mitochondrial dysfunction, implicating a causal role for secondary mitochondrial DNA defects in disease pathophysiology.

Conclusion:
Additional neuromuscular features are common in patients with *OPA1* mutations and careful surveillance is therefore mandatory to optimise the detection and management of neurological disability in a group of patients with already significant visual impairment.

References:
1. Newman NJ, Biousse V. Hereditary optic neuropathies. Eye 2004;18:1144-60.
2. Yu-Wai-Man P, Griffiths PG, Hudson G, Chinnery PF. Inherited mitochondrial optic neuropathies. Journal of Medical Genetics 2009;46:145-58.
3. Amati-Bonneau P, Valentino ML, Reynier P, Gallardo ME, Bornstein B, *et al*. *OPA1* mutations induce mitochondrial DNA instability and optic atrophy plus phenotypes. Brain 2008;131:338-51.
4. Hudson G, Amati-Bonneau P, Blakely EL, Stewart JD, He LP, *et al*. Mutation of *OPA1* causes dominant optic atrophy with external ophthalmoplegia, ataxia, deafness and multiple mitochondrial DNA deletions: a novel disorder of mtDNA maintenance. Brain 2008;131:329-37.

Key Words: Dominant optic atrophy, Inherited optic neuropathy, Mitochondrial genetic disorders, Hereditary spastic paraplegia, Multiple sclerosis

Financial Disclosure: NONE

8:30 a.m. - 8:45 a.m.

Undiagnosed Idiopathic Intracranial Hypertension in a Population of Morbidly Obese Patients: A Prospective Study

Claudia Krispel[1], William Smith[2], David Chu[1], Mohamed Ali[2], John Keltner[1]

[1]University of California at Davis, Eye Center, Sacramento, CA, United States, [2]University of California at Davis, Department of Surgery, Sacramento, CA, United States

Introduction:
Idiopathic intracranial hypertension (IIH) is a relatively rare condition, the annual incidence of which is approximately 1 to 2 per 100,000[1] based on various studies from different countries. Obesity increases the incidence to 19 per 100,000[1,2]. One study suggested that as many as 25% of patients diagnosed with IIH may be asymptomatic[3]. The purpose of the present study is to determine the incidence of undiagnosed or asymptomatic IIH in a population of morbidly obese individuals.

Methods:
All morbidly obese patients presenting to the UC Davis bariatric surgery clinic between February 2008 and September 2009 who consented to the study and had no visual opacity preventing high quality fundus photos were included in the study. Participants were screened for papilledema by nonmydriatic fundus photos or by symptoms concerning for IIH prompting direct referral for neuro-ophthalmologic evaluation. Nonmydriatic fundus photos were reviewed by a UC Davis neuro-ophthalmologist, and patients with optic discs suspicious for edema were brought in for neuro-ophthalmologic evaluation. Patients with findings consistent with IIH were sent for neurologic evaluation and treatment of IIH if indicated.

Results:
To date 449 obese individuals (96 men, 353 women) have been screened. 23 of these patients were excluded from the study due to insufficient quality of the nonmydriatic fundus photos. The included patients had an average BMI of 47. Four out of 426 patients (approximate annual incidence of 560 per 100,000) were found to have subtle optic disc edema and were referred for full neurologic IIH workup. All 4 patients had normal MRIs; 3 underwent lumbar punctures with borderline or slightly high opening pressures suggesting mild IIH.

Conclusion:
The incidence of early undiagnosed or asymptomatic IIH appears to be significantly higher in a morbidly obese patient population compared to estimates of the overall incidence of IIH in the general population.

References:
1. Radhakrishnan K, Ahlskog J, Garrity J, Kurland L. Idiopathic intracranial hypertension. *Mayo Clin Proc* 69:169-180, 1994.
2. Durcan FJ, Corbett JJ, Wall M. The incidence of pseudotumor cerebri. Population studies in Iowa and Louisiana. *Arch Neurol* 45:875-877, 1988.
3. Galvin JA, Van Stavern GP. Clinical characterization of idiopathic intracranial hypertension at the Detroit Medical Center. *J Neurol Sci* 223(2):157-160, 2004.

Key Words: idiopathic intracranial hypertension, IIH, pseudotumor cerebri, obesity, bariatric surgery

Financial Disclosure: NONE

8:45 a.m. - 9:00 a.m.

Correlating Retinal Nerve Fiber Layer Atrophy, Diffusion Tensor Imaging, and Functional Outcomes after Optic Neuritis

Fiona Costello, Bradley Goodyear, Yunyan Zhang, James Scott, Nourhan Zayed, Jessie Trufyn

University of Calgary, Calgary, Alberta, Canada

Introduction:
The aim of our study was to explore the relationship between retinal nerve fiber layer (RNFL) thickness, diffusion tensor imaging (DTI) and visual outcomes after acute optic neuritis (ON).

Methods:
In this prospective cohort study, 9 patients (8 females, average age 36 years) with acute ON were followed for 6-months. Baseline RNFL and macular volumes (MV) (Zeiss Stratus III), DTI images (acquired with 3T MRI), visual acuity, visual field mean sensitivity and low contrast letter acuity measures were compared at baseline and in follow up. DTI measures including apparent diffusion coefficient (ADC) and fractional anisotropy (FA) were also obtained.

Results:
The average RNFL measurements in ON eyes were significantly lower at 6-months (ON eyes = 87.9µm; unaffected eyes 98.1µm) than baseline (109.9µm; 101.9µm) ($p < 0.0001$). Similarly, baseline MV in ON eyes (6.57mm^3) was decreased in follow up (6.17mm3) ($p < 0.001$). Mean fractional anisotropy was reduced acutely in ON eyes (0.3953) and in follow up (0.3773) relative to unaffected eyes (baseline FA = 0.3889; 6-months = 0.4016), but differences did not reach statistical significance ($p = 0.069$). Significant correlations were noted between RNFL atrophy and visual outcomes, but not for ADC or FA values in our small study population.

Conclusion:
RNFL and macular volumes provide structural correlates, which may complement functional outcome measures after acute ON. DTI may contribute more data by showing loss of anisotropy after ON, but further prospective studies are needed to establish the broad applications of non-conventional MRI techniques in the care of MS patients.

References: NONE

Key Words: Retinal Nerve Fiber Layer, Diffusion Tensor Imaging, Optic Neuritis, Multiple Sclerosis, Optical Coherence Tomography

Financial Disclosure: NONE

9:00 a.m. - 9:15 a.m.

Transplantation of Differentiated Embryonic Stem Cells for Re-Population of Retinal Ganglion Cells in the Adult

Y. Joyce Liao, Yi-Wen Chen, James Weimann, Lawrence Recht

Stanford University, Stanford, United States

Introduction:
The mammalian central nervous system has limited regenerative abilities. As a result, injury and disease typically lead to irreversible neuronal loss and permanent functional impact. Stem cell transplantation, despite being in its infancy, promises the greatest potential for re-population and re-engineering of neural circuit. Embryonic stem (ES) cells are totipotent cells that can undergo unlimited self-renewal and differentiate into any adult cell type. We have previously injected differentiated ES cells into the visual cortex, which led to prominent axon projections to the dorsal superior colliculus, which is important for pupillary response and visually guided behavior. Next, we tackled regenerative therapy to replenish retinal ganglion cells.

Methods:
We grew enhanced green fluorescent protein-positive ES cells on a confluent layer of MS5 cells. After 6 days of co-culture, we generated colonies of neural precursor cells, with few cells expressing Oct3/4 (an ES cell marker), 80% expressing nestin (proliferative marker), and 30% expressing class-III beta-tubulin, an early marker for retinal ganglion cells. We transplanted differentiated ES cells into adult wild-type mice and performed morphometric analyses.

Results:
We found that compared to subretinal injection, intravitreal injection was technically easier and led to superior transplantation efficacy. Transplantation was also enhanced by induction of retinal fate by treating ES cells at days 1 and 3 with noggin, a BMP inhibitor, and dkk1, a Wnt inhibitor. Lastly, retina lasering, a technique already well established in humans for treatment of diabetic retinopathy and other diseases, dramatically enhanced stem cell survival and caused elaboration of neurite-like processes which extended over 800-microns from the peripheral retina to the optic nerve head.

Conclusion:
Regenerative therapy using embryonic stem cells is feasible in adult mammals. Different techniques, including intravitreal injection of retinal progenitors and retina lasering provide a permissive environment for robust stem cell survival and extension of processes.

References: NONE

Key Words: stem cell, retinal ganglion cell, laser, transplantation

Financial Disclosure: NONE

10:00 a.m. - 10:15 a.m.

Absent Trochlear Nerve and Superior Oblique Hypoplasia in Patients with Congenital Superior Oblique Palsy

Jeong-Min Hwang, Jae Hyoung Kim

Department of Ophthalmology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

Introduction:
In order to elucidate the pathogenic mechanism of congenital superior oblique palsy by evaluating the appearance of the superior oblique muscle and trochlear nerve on magnetic resonance (MRI).

Methods:
Ophthalmologic examination and thin-sectioned MRI at the brainstem level as well as across the orbit, were performed in 19 patients with congenital superior oblique palsy. To confirm the accuracy of the procedure, we compared the results obtained with those of a control group of 12 children using the same technique.

Results:
Eleven patients showed a definite hypoplasitic superior oblique muscle and absent trochlear nerve on the affected side. One patient showed absent trochlear nerve on the affected side and symmetric normal-sized superior oblique muscles. Remaining seven patients showed symmetric normal-sized superior oblique muscle and trochlear nerves were present in both sides. The trochlear nerves as well as normal-sized superior oblique muscles were observed in 24 (100%) of 24 eyes screened as controls.

Conclusion:
Congenital superior oblique palsy could be classified as three groups according to the superior oblique hypoplasia and the presence of the trochlear nerve. Congenital aplasia of the trochlear nerve was the most common underlying pathology of congenital superior oblique palsy.

References: NONE

Key Words: magnetic resonance imaging, congenital trochlear nerve palsy, congenital superior oblique palsy, superior oblique hypoplasia, absence of trochlear nerve

Financial Disclosure: NONE

10:15 a.m. - 10:30 a.m.

Visual Field Profile of Optic Neuritis: A Final Follow-Up Report from the Optic Neuritis Treatment Trial (ONTT) from Baseline to 15 Years

John Keltner[1], Chris Johnson[2], Kimberly Cello[1], Robin Gal[3], Roy Beck[3]

[1]UC Davis Department of Ophthalmology & Vision Science, Sacramento, CA, United States, [2]University of Iowa Department of Ophthalmology and Visual Sciences, Iowa City, IA, United States, [3]Jaeb Center for Health Research, Tampa, FL, United States

Introduction:
To evaluate visual field abnormalities after an episode of optic neuritis in Optic Neuritis Treatment Trial (ONTT) patients.

Methods:
Three readers independently evaluated 10,443 visual fields from 454 patients with available data over 15 visits (visits 1-8 [within the first year] and single visits for years 1 – 5, 10 and 15). The readers classified visual field abnormalities into 21 different monocular categories representing three general types of visual loss (diffuse, localized and artifactual). Classification frequency was determined and reader agreement was evaluated. The association of visual field abnormality classifications with Mean Deviation, Pattern Standard Deviation, Visual Acuity, and Foveal Threshold were assessed.

Results:
At baseline, 66.2% of the abnormalities in the affected eyes consisted of diffuse loss (includes central and centrocecal loss) while only 6.2% of the abnormalities in the fellow eyes consisted of the diffuse loss. During years 1 – 15, the affected and fellow eyes exhibited predominantly localized loss in the nerve fiber bundle region (partial arcuate, paracentral, and arcuate defects). At Year 1, 35.7% of the abnormalities in the affected eyes and 34.4% in the fellow eyes consisted of localized defects. At Year 15, 39.5% consisted of localized defects in the affected eyes and 26.3% were localized deficits in the fellow eyes. Foveal threshold was highly correlated with visual acuity and contrast sensitivity in the affected eye at baseline (-0.82, 0.79, respectively), 6 months (-0.84, 0.81, respectively) and 1 year (-0.84, 0.79, respectively).

Conclusion:
Diffuse and central loss was more predominant in the affected eye at baseline, and nerve fiber bundle defects (partial arcuate, paracentral and arcuate) were the most predominant localized abnormalities in both the affected and fellow eyes over the course of the study.

References:
1. Keltner JL, Johnson CA, Spurr JO, Beck RW, and the Optic Neuritis Study Group. Baseline Visual Field Profile of Optic Neuritis. Arch Ophthal. 1993;111:231-234.
2. Keltner JL, Johnson CA, Spurr JO, Beck RW, and the Optic Neuritis Study Group. Visual Field Profile of Optic Neuritis: One-Year Follow-up in the ONTT, Arch Ophthal. 1994;112:946-953.
3. The Optic Neuritis Study Group, Multiple Sclerosis Risk After Optic Neuritis, Arch Neurol. 2008;65(6):727-732.
4. Keltner JL, Johnson CA, Cello KE, Dontchev M, and Gal RL, Visual Field Profile of Optic Neuritis: A Final Follow-up Report from the ONTT from Baseline to 15 Years, Arch Ophthal. IN PRESS

Key Words: visual fields, optic neuritis, multiple sclerosis

Financial Disclosure: NONE

10:30 a.m. - 10:45 a.m.

Reference Range of Cerebrospinal Fluid Opening Pressure in Children

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

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

Introduction:
The normal range of cerebrospinal fluid (CSF) opening pressure (OP) obtained during lumbar puncture (LP) has not been established in children. Preliminary data from our center proposed a reference range for CSF OP higher than what has been listed in textbooks. Based on our completed prospective study, we propose a CSF OP reference range in children according to age group.

Methods:
This is a single center prospective study of CSF OP performed at an urban, tertiary care children's hospital from 1/15/2007 to 2/28/2009. Subjects 1 – 18 years of age were included if their OP (cm H_2O) was measured during LP prior to removal of CSF. Patients with factors believed to alter OP [i.e., agitation during LP, presence of papilledema, diseases/medications (i.e., meningitis, elevated CSF protein, acetazolamide)] were excluded from analysis. Subjects were divided into 4 age groups (1-4, 5-9, 10-14 and 15-18 years). Median and 95^{th} percentiles of OP were calculated for each age group.

Results:
1,066 subjects were screened and 491 were eligible for enrollment. 472 were enrolled and 439 were successful in obtaining an OP. 274 enrolled patients were excluded since they had clinical factors believed to alter their ICP, leaving 165 patients to calculate the reference range. Median and 95th percentile (in parenthesis) OP, based on age group, were calculated: 1-4 years: 18(32); 5-9 years: 18(25); 10-14 years: 19.3(30); 15-18 years: 21(29.2). Linear regression analysis revealed OP was influenced by body mass index only in the oldest age group ($p = 0.001$).

Conclusion:
To our knowledge, this is the first prospective study which systematically defines a reference range of CSF OP in children. In each age group, the OP median and range were higher than listed in common textbooks. An OP above the 95^{th} percentile for each age group (32, 25, 30, and 29.2, respectively) should be considered abnormal.

References: NONE

Key Words: lumbar puncture, opening pressure, cerebrospinal fluid, idiopathic intracranial hypertension,

Financial Disclosure: NONE

10:45 a.m. - 11:00 a.m.

The use of the Pipeline Embolization Device (PED) in the Treatment of Complex Symptomatic Cavernous and Paraophthalmic Segment Aneurysms of the Internal Carotid Artery (ICA): An Interim Analysis with 6 Month Follow-up of Neuroophthalmologic and Angiographic Outcomes

Mohammad Fouladvand, Kathleen McConnell, Tibor Becske, Peter Kim Nelson

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Introduction:
Complex cavernous and paraophthalmic segment aneurysms of the ICA present distinct challenges for definitive parent-vessel sparing neuroendovascular treatment. The 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 hemodynamically alter intra-aneurismal flow, promoting intra-saccular hemostasis and aneurysm thrombosis without the need for coil embolization. PED offers significantly improved occlusion rates over conventional stent/coil techniques; and, by averting the need for intraaneurismal coils, permits more complete resolution of mass effect- with the attendant improvement in neurologic symptoms referable to the aneurysm.

Methods:
30 patients (27F:3M, mean age 59.8 years) with large cavernous and proximal supraclinoidal segment carotid aneurysms were treated with PED as part of a prospective, single-arm trial. Each patient underwent neuroophthalmologic evaluation prior to treatment and at 6 months by a neuroophthalmologist blinded to aneurysm location and size. Follow-up angiographic assessment of the aneurysm was obtained at 6 months. We now report an interim analysis of the initial 12 patients treated by us who have completed their 6 month follow-up exams. Follow-up for the remaining 18 patients is ongoing.

Results:
Of the 12 patients followed to date, mean maximum aneurysm dimension was 19.7mm (10.9-32.5). Average duration of symptoms: 1.5 years (0.34-3.25). Of 5 patients presenting with aneurysm associated pain (mean initial pain score: 7.2 out of 10 [4-9]), at six months follow-up only one patient reported any residual pain (pain score 2). 7 patients presented with optic neuropathies (APD) of which 3 improved at 6 months. 3 presented with oculomotor neuropathies of which 2 improved. 6 presented with abducens palsy of which 5 improved. Follow-up angiography confirmed occlusion of all 12 aneurysms.

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

References: NONE

Key Words: Pipeline Embolization Device, Cavernous segment aneurysms, para-ophthalmic segment aneurysms, cranial neuropathies, endovascular

Financial Disclosure: NONE

11:00 a.m. - 11:15 a.m.

The Value of MRI in the Diagnosis of Giant Cell Arteritis

Randy Kardon[1], Paul Wheeler[2], Fabiana Policeni[1], Joan Maley[2]

[1]University of Iowa College of Medicine and Department of Veterans Affairs, Ophthalmology, Iowa City, IA, United States, [2]University of Iowa College of Medicine, Dept Neuro-radiology, Iowa City, IA, United States

Introduction:
Specific MRI enhancement of the arterial wall occurs in patients with giant cell arteritis (GCA). A retrospective study was performed to determine the sensitivity and specificity of MRI findings in patients undergoing temporal artery biopsy.

Methods:
MRI scans were evaluated independently in biopsied patients who were divided into those with a clinical diagnosis of GCA based on biopsy, laboratory testing, and symptoms and those without GCA,

Results:
21 patients had both a temporal artery biopsy and an MRI scan (fat suppression with gadolinium). 8/10 patients had positive MRI findings with a diagnosis of GCA and 7/11 patients without GCA had negative MRI findings. Specific MRI criteria of transmural wall enhancement with gadolinium were developed for making a radiologic diagnosis of GCA.

Conclusion:
The sensitivity of MRI findings in GCA was 80% and specificity was 64 %. The study was limited by the small number of patients undergoing both temporal artery biopsy and MRI and the uncertainty of a GCA diagnosis in some cases. The prospective use of MRI in directing the biopsy location and in the diagnosis of GCA is being studied presently.

References:
1. Bley, et al. High-resolution MRI in giant Cell Arteritis: Imaging of the wall of the superficial temporal artery. AJR: 184, 283-287, 2005.
2. Bley, et al. 3-T MRI reveals cranial and thoracic inflammatory changes in giant cell arteritis. Clin Rheumatology, 26, 448-450, 2007.
3. Bley, et al. Integrated head-thoracic MRI at 3T: Assessment of cranial ,cervical and thoracic involvement of giant cell arteritis. MAGNA, 18, 193-200, 2005
4. Bley, et al. Influence of corticosteroid treatment on MRI findings in giant cell arteritis. Clin Rheumatology, 26, 1541-1543, 2007.
5. Bley, et al. Mural inflammatory hyper enhancement MRI of giant cell arteritis resolves under corticosteroid treatment. Rheumatology, 47, 65-67, 2008
6. Mark, et al. High resolution 3T MRI for the cervical and superficial cranial arteries in giant cell arteritis. Journal of Magnetic Resonance Imaging, 24, 423-427, 2006.

Key Words: Giant Cell Arteritis, MRI, Temporal Arteritis

Financial Disclosure: NONE

11:15 a.m. - 11:30 a.m.

One Eye or Two: the Advantage and Significance of Binocular Low-Contrast Acuity Testing in Multiple Sclerosis

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Introduction:
Binocular low-contrast acuity (LCA) and high-contrast visual acuity (HCA) have been used extensively in MS clinical trials. Monocular testing has been added to provide structure-function correlations with optical coherence tomography (OCT). We examined the relation of binocular LCA and HCA to monocular acuities and quality of life (QOL), and determined factors that impact binocular summation, the extent to which binocular acuities are better than monocular scores for better eyes.

Methods:
LCA and HCA were assessed binocularly and for each eye separately in MS patients and disease-free controls at three centers. Binocular summation was defined as the difference, if >0, between the binocular letter score and the monocular score for the better eye. The relation of binocular scores and degrees of summation to better and worse eye vision, prior history of optic neuritis (ON), and NEI-VFQ-25 QOL scores was determined.

Results:
Binocular summation was captured better by LCA than HCA for MS (n=774) and controls (n=268). Summation was more frequent among patients with no history of ON. Older age, prior ON history, and increased inter-ocular difference (threshold 5-7 letters) were associated with binocular *inhibition* (binocular<better eye). Compared with better or worse eyes, binocular acuities demonstrated stronger correlations with NEI-VFQ-25 composite scores ($p<0.001$); this scale also correlated well with binocular summation. Gradual declines in binocular LCA line scores with decreasing letter sizes were as noted in MS, but not in controls.

Conclusion:
Binocular acuity measurements are enhanced by summation. This is hindered in MS patients with a history of ON, increasing age, and inter-ocular acuity differences, explaining, in part, why patients may prefer to close an eye with monocular vision loss. Patterns of LCA decline with decreasing letter size suggest a central processing component to binocular LCA. Binocular acuities best reflect QOL, and should be considered a primary measure of visual function for clinical trials.

References:
1. Azen, SP, Varma, R, Preston-Martin, S, Ying-Lai, M, Globe, Denise, Hahn, Sora. "Binocular visual acuity summation and inhibition in an ocular epidemiological study: the Los Angeles Latino Eye Study." IOVS 43, 1742-1748, 2002.
2. Gagnon, R, Kline, D. "Senescent effects on binocular summation for contrast sensitivity and spatial interval acuity",Current Eye Research, 27, 315 -321, 2003.
3. Simpson, WA, Manahilov, V, Shahani, U. "Two eyes: √2 better than one?" Acta Psychologica 131, 93-98, 2009.
4. Wu, GF, Schwartz, ED, Lei, T, Souza, A, Mishra, S, et al. "Relation of vision to global regional brain MRI in multiple sclerosis." Neurology 69, 2128-2135, 2007.

Key Words: binocular summation, low contrast acuity, optic neuritis, multiple sclerosis, binocular function

Financial Disclosure: NONE

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

Superior Oblique Myokymia: Evidence for a Trochlear Neuropathy

Yi-Ren Chen, Sumeer Thinda, Y. Joyce Liao

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Introduction:
Superior oblique myokymia (SOM) is an oculomotor disorder characterized by unilateral, intermittent contractions of the superior oblique muscle resulting in oscillopsia and diplopia[1]. The pathogenesis may involve trochlear nucleus abnormalities, lesions in the infranuclear tract, or microvascular compression of the trochlear nerve by branches of the posterior cerebral or superior cerebellar artery at the root exit zone[1,2].

Methods:
We used 60-Hz three-dimensional and 500-Hz two-dimensional infrared oculography to characterize fixation and centrifugal saccades in 4 patients with SOM. All patients were consented per protocol approved by the Institutional Review Board.

Results:
All patients exhibited episodic 0.5-4 deg intorsion of the affected eye in primary gaze. These events lasted 1-50 seconds and occurred at <1 to 5 Hz. Eccentric gazes worsened or improved torsional nystagmus, with direct correlation with the activity of the superior oblique muscle. Depression or abduction of the affected eye, movements that require the superior oblique muscle, triggered increased nystagmus amplitude, while adduction and elevation, movements that do not require activation of the superior oblique muscle, led to amelioration of the torsional nystagmus. In all 4 patients, downward saccade triggered the worst intorsion (5-10 deg, $p = 0.004$) and torsional nystagmus. In one patient, we used 500-Hz infrared oculography to analyze centrifugal reflexive saccades. In contrast to that expected in trochlear nerve palsy, downward saccades by a SOM patient exhibited supranormal amplitudes in the affected eye compared to the unaffected eye ($p = 0.007$). There was no inter-ocular difference in saccade amplitudes on supraduction. Interestingly, in the absence of visual cues, patients exhibited initial torsional nystagmus followed by gradual extorsion and elevation of the affected eye and resolution of nystagmus. All patients improved with conservative treatment including stress reduction and use of neuropathic and membrane-stabilizing medications including carbamazepine, oxcarbamazepine, and clonazepam.

Conclusion:
Our recordings provided compelling evidence in support of a SOM as a neuropathic process related to cranial nerve IV injury followed by aberrant regeneration.

References:

1 Kattah JC, FitzGibbon EJ. Superior oblique myokymia. Curr Neurol Neurosci Rep. 2003;3(5):395-400.

2 Komai K, Mimura O, Uyama J, Takubo K, Kaisho Y, Izaki A et al. Neuro-ophthalmological evaluation of superior oblique myokymia. Neuro-Ophthalmology. 1992;12(3):135-140.

Key Words: superior oblique myokymia, nystagmus, diplopia, cranial nerve,

Financial Disclosure: NONE

11:45 a.m. – 12:00 p.m.

Non-Mydriatic Fundus Photography in the Diagnosis of Acute Neuro-Ophthalmic Disease in the Emergency Department (ED)

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Introduction:
Visualization of the ocular fundus remains a critical part of the screening physical examination for numerous patients in the ED. Our objective was to determine if non-mydriatic fundus photography taken by nurse practitioners (NPs) and interpreted by neuro-ophthalmologists is superior to direct ophthalmoscopy as performed by ED physicians.

Methods:
Interim analysis of 200/350 planned, prospectively enrolled, consecutive patients seen in a university hospital ED with a chief complaint of headache, acute focal neurologic dysfunction, diastolic blood pressure >120 mmHg, or vision loss. Non-mydriatic photography of both eyes was obtained by NPs during their usual ED shift in the triage area and interpreted by two neuro-ophthalmologists within 24 hours. Urgent findings were defined as disc edema, disc pallor, intraocular hemorrhage, retinal whitening, severe vascular retinopathy, retinal vascular emboli or occlusion. Performance and outcome of direct ophthalmoscopy by ED physicians (masked to the fundus photography results) was systematically recorded.

Results:
ED physicians performed direct ophthalmoscopy on 33/200 (17%) of enrolled patients. 31/200 (16%) of patients had an urgent finding identified by a neuro-ophthalmologist on fundus photographs. The ED physicians performed direct ophthalmoscopy on 10/31 (32%) of patients with urgent findings but only identified one of these urgent findings. An additional 12 (39%) of the urgent findings were identified by consultation with other services, but 18 (58%) were not identified during the course of routine ED care (and would have been undiagnosed in the absence of non-mydriatic fundus photography).

Conclusion:
ED physicians do not use the direct ophthalmoscope systematically; when they do examine the fundus by direct ophthalmoscopy, they almost always miss relevant findings. Even with 24 hour availability of on-call ophthalmologists, over half of urgent findings are missed. Fundus photography taken by NPs and interpreted by neuro-ophthalmologists by a telemedical approach is superior for the detection of urgent neuro-ophthalmic diagnoses in the ED.

References: NONE

Key Words: non-mydriatic photography, emergency department, direct ophthalmoscopy, diagnosis of neuro-ophthlamic disease, telemedicine

Financial Disclosure: NONE