Pathogenesis role of hydrodynamic of eye in traumatic optical neuropathy

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Introduction:
The value of eye hydrodynamics and interaction between eye and head pressures circulation fluids between the eyes on the affected side and on the opposite the development of traumatic lesions of the optic nerve need more careful study.

Methods:
21 patients with TON were examined, using by visometry, ophthalmoscopy and perimetry, Nesterov’s tonographia.

Results:
The magnitude of the coefficient of outflow of intraocular fluid (C) revealed 4 groups of injured:with bilateral decreased outflow (two sided C <0.3 mm³/min/mm Hg) - 5 patients (23.81%);strengthening of bilateral (two sided C ≥ 0.3 mm³/min/mm Hg) – 4 (19.05%);increased outflow from side damage and weakening on the opposite side (IL C ≥ 0.3 mm³/min/mm Hg CL C <0.3 mm³/min/mm Hg) - 5 (23.81%);weakening of the outflow on the affected side and increased on the opposite side (IL p <0.3 mm³/hv/mm.rt.st., CL C > 0.3 mm³/min/mm Hg) - 7 (33.33%).
The magnitude of C lowest acuity 0.73 ± 0.36 on the affected side for bilateral decrease in performance. Proportion of patients with reduced visual acuity was also highest in this group and was 75.0% (3 injured, n = 4). The sum of the field of view to white on the affected side was slightly lower than the opposite and was 201.15 ± 40.93⁰ and 222.69 ± 17.63⁰ respectively. The lowest amount was determined in patients with weakening outflow on the affected side and increased on the opposite side, which was marked bilateral narrowing of the field of view at 105.89 ± 36.37⁰ on injured side and 78.04 ± 7.31⁰ contralateral place primary lesion in comparison with the control group (p <0.05).

Conclusions:
Hydrodynamic's changes may case secondary lesion of the optic nerve.

References:
Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), CSF (Intracranial Hypertension, Intracranial Hypotension, etc)

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83 (Submitted)
The molecular and neuro-ophthalmological features of autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS)

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Introduction:
The inherited ataxias and spastic paraplegias are genetically highly heterogeneous and reaching a confirmed molecular diagnosis remains challenging. Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a relatively rare subtype that was first described among French Canadian patients from Québec presenting with a stereotypical triad of early-onset cerebellar ataxia, spastic paraplegia and peripheral neuropathy. Pathogenic mutations in the SACS gene were subsequently identified in these families. Although retinal hypermyelination was originally reported as a characteristic disease manifestation, the actual nature and frequency of these abnormal retinal findings in ARSACS has recently been disputed.

Methods:
Next-generation exome sequencing was used to investigate a cohort of 50 probands with suspected inherited ataxia and spastic paraplegia syndromes. A comprehensive neuro-ophthalmological examination, including high-resolution optic coherence tomography (OCT) imaging, was carried out on patients with confirmed pathogenic SACS mutations.

Results:
Pathogenic SACS mutations were identified in three probands and two additional affected family members were examined. Compared with patients from Québec, our ARSACS cohort (n = 5) showed strikingly variable features with a delayed age of onset and a milder neurological phenotype. Eye movement abnormalities were common with ocular dysmetria and gaze-evoked nystagmus. None of our patients had evidence of retinal hypermyelination. However, retinal striations were observed around the optic discs in four patients with significant thickening of the peripapillary retinal nerve fiber layer (RNFL).

Conclusions:
Next-generation exome sequencing is a powerful diagnostic tool that is broadening the disease phenotype associated with specific mutations. Abnormal retinal thickening seems to be a common pathological feature among affected SACS mutation carriers. A dilated fundus examination and OCT imaging should therefore be considered in patients with unexplained multisystem neurological disease. When present, retinal striations and RNFL thickening raises the distinct possibility of ARSACS and SACS genetic screening should be considered.
Grant Support: Medical Research Council (MRC, UK) and the Wellcome Trust (UK)

References:


Keywords: Systemic Disease, Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), YES

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85 (Submitted)
Visual Recovery and Optical Coherence Tomography (OCT) Changes Following Treatment of Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) with Levodopa Alone or in Combination with Allopurinol and Tetracycline

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Introduction:
To determine the effectiveness of levodopa alone or in combination with allopurinol and tetracycline on visual acuity, visual field, and retinal nerve fiber layer (RNFL) thickness in eyes affected by NAION.

Methods:
Retrospective cohort study involving 33 eyes of 33 patients, from 119 consecutively evaluated patients with NAION. Patients evaluated within 45 days of NAION onset and who had at least one OCT within 1 year of NAION onset were enrolled. Patients had received treatment with levodopa alone (Levodopa only) or in combination with allopurinol and tetracycline (Levodopa combined). Best corrected visual acuity converted to logMAR, mean deviation (MD) threshold sensitivity on automated perimetry, and RNFL thickness on OCT were recorded. Primary outcome measures were changes in logMAR visual acuity, MD threshold sensitivity, and RNFL thickness within 1 year of NAION onset.

Results:
Among patients with visual acuity of 20/60 or worse, improvement by 3 or more lines was documented for 71% (5 of 7) of Levodopa only and 50% (4 of 8) of Levodopa combined participants. No patient had worsened visual acuity. There was no significant difference (p=0.91) between the change in visual acuity for Levodopa only (-0.43 logMAR) and Levodopa combined (-0.4 logMAR). There was no significant difference (p=0.9) between the change in MD threshold sensitivity for Levodopa only (1.79 dB) and Levodopa combined (1.54 dB). The average RNFL thickness at 5 months decreased by 23.6% for patients treated with levodopa, in contrast with previously published reports which documented decrease in average RNFL thickness of 35 to 42% for untreated patients.
Conclusions:
Treatment within 45 days of onset of NAION with levodopa alone or in combination with allopurinol and tetracycline improved visual acuity but not visual field. Levodopa may promote neuroprotection in NAION by decreasing retinal ganglion cell loss and subsequent RNFL thinning.

References:
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Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Nerve Fiber Layer and Retinal Testing (OCT, ERG Etc), YES

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86 (Submitted)
MRI-based structural analysis of pituitary tumors: A critical review of literature on the clinico-radiographic paradox

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Introduction:
Pituitary tumors are one of the most common types of brain tumors that can cause progressive blindness. Due to the indolent nature of the vision loss, these patients are often misdiagnosed which can turn a reversible cause of visual dysfunction into a permanent life-altering disability. Currently, magnetic resonance imaging (MRI) is the central diagnostic tools that guide the treatment planning. An ongoing challenge to the management of patients with pituitary tumors is the cost, availability and reliability of current MRI techniques to capture clinically significant incremental tumor growth. The purpose of this study was to perform a critical review of literature on the proposed MRI-based structural analyses of pituitary tumors and the structure-function relationship of the visual pathway.

Methods:
A critical review was performed of all literature that discussed MRI-based structural analyses of pituitary adenomas using PubMed, Embase, Cochrane Library and Google Scholar. All studies published from January 1990 to August 2013 were eligible for inclusion. Search terms used were: “pituitary gland”, “pituitary neoplasm”, “pituitary surgery”, “magnetic resonance imaging”, “visual field”, “visual acuity”, “vision”, “visual test”, “vision disorders”, “optic nerve”, “optic chiasm”, and “visual pathway”.

Results:
A total of 443 citations were retrieved from our search strategy and review of bibliographies. Eight of these studies met inclusion/exclusion criteria and were retrieved for critical review. All 8 of these studies were published between 1995 and 2011; most studies were published after 2006. Only one structural predictor of visual recovery were identified in these studies: severity of optic atrophy.

Conclusions:
While MRI-based structural analyses is an important and useful tool for managing patients with pituitary tumors, there are limited objective measures shown to be predictive of post-operative visual recovery.

Keywords: Neuro-Imaging (MRI, CT, etc), Anterior Afferent Visual Pathway (Optic Neuropathy and
87 (Submitted)
MRI vs. OCT: Do structural analyses predict visual recovery in compressive pituitary tumors?

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Introduction:
Clinically relevant pituitary lesions affect approximately 1/1000 people. For patients with associated vision loss, the optimal surgical treatment window is not known and there are no validated predictors of visual recovery. The purpose of this study was to determine whether two commonly utilized structural analyses of the visual pathway differentiated patients with poor visual outcomes after surgery from those with good visual recovery.

Methods:
18 patients (11 females, mean age 52 years) with visually significant pituitary macroadenomas underwent a neuro-ophthalmic evaluation and spectral-domain optical coherence tomography (OCT) testing pre-operatively and 6-months after surgery. Pre-operative RNFL thickness (RNFL), and macular volume, (MV) were compared between patients with normalized visual function versus persistent visual deficits after surgery. Pre-operative measures of optic nerve compression and chiasm elevation also were compared between patients with normalized visual function versus persistent visual deficits after surgery (visual acuity ≤ 20/40; visual field mean deviation ≤ -5.0 decibels).

Results:
After 6- months, only 54% of patients with normal visual outcomes reported awareness of vision loss at onset, as compared to 88% of patients with poor visual recovery after surgery. Pre-operative RNFLT (72 vs 84μm; p = 0.01) and MV (9.2 vs 10.0mm3; p = 0.0007) were significantly lower in patients with poor outcomes relative to patients with normal vision after surgery. Patients with poor visual outcome also had greater optic nerve compression than those with improvement in visual function.

Conclusions:
Structural changes seen in the anterior visual pathway may provide new predictive measures of visual outcomes after surgical resection of compressive pituitary tumor.

Grant Support:

Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Nerve Fiber Layer and Retinal Testing (OCT, ERG Etc), YES

Financial Disclosures: The authors had no disclosures.
Incidence of Giant Cell Arteritis: Diabetes Mellitus is Not Protective

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Introduction:
Previous reports suggest a protective effect of diabetes mellitus (DM) against giant cell arteritis (GCA). One recent retrospective study found a lower prevalence of diabetes among patients with a positive temporal artery biopsy (TAB) than with a negative TAB. A meta-analysis of 8 studies found a low prevalence of biopsy positive GCA among diabetics. The authors suggested that DM may lower the risk of GCA. To our knowledge, the effect of DM on GCA has not been studied prospectively. Using the Medicare database, we followed historical patients prospectively through time to compare the incidence of GCA among patients with and without diabetes.

Methods:
A 5% sample of Medicare claims and enrollment data from 1994-2011 was analyzed. Patients with diabetes were defined as those with a diagnosis code of 250.xx. GCA was defined as 1) any subject who received a GCA diagnosis (ICD9 446.5) following a TAB (CPT 37609), or 2) any patient who received two GCA diagnoses (ICD9 446.5) within 180 days. A three-year look-back period during which a diagnosis of GCA was not observed was required for inclusion in the study. A combination of propensity score matching and competing-risk regression was used to assess the impact of DM on GCA. To optimize propensity score matching, patients under 68 years were excluded.

Results:
A total of 151,041 individuals with diabetes were matched to an equal number of controls. Mean study time was 67.39 months for diabetics and 68.11 months for controls. GCA was diagnosed among 1,116 patients with diabetes (0.73%) versus 465 (0.30%) controls. The risk of GCA diagnosis among patients with diabetes was increased by 100% (sub hazard ratio (SHR): 2.00; 95% confidence interval (CI): 1.78 2.25).

Conclusions:
Diabetes mellitus is not protective against GCA. The annual incidence of GCA diagnosis among individuals 68 and over was 9 in 10,000.

References:

Keywords: Systemic Disease, Miscellaneous, YES

Financial Disclosures: The authors had no disclosures.
Introduction:
Pelizaeus-Merzbacher disease is an X-linked recessive neurological disorder with nystagmus, ataxia, spasticity and developmental delay. It is linked to a diffuse hypomyelination of the central nervous system due to mutations in the PLP1 gene with abnormal expression of the proteolipid membrane protein PLP in the central nervous system. Progression of clinical signs is related to age of onset of the disease. Initially, an irregular pendular nystagmus is always present without affecting visual function. Fundus appearance remains normal. Cortical flash visual evoked potentials (flash-VEPs) are typical for hypomyelination. Nystagmus may disappear between the age of 2 to 5 years while optic atrophy later develops.

Methods:
A 14-year-old boy presented with Pelizaeus-Merzbacher disease. He had been suffering from that condition for several years. At the time of examination, he was in a wheelchair but could stand up with difficulty and demonstrated an obvious psychomotor delay. He was subsequently shown to carry a mutation in the PLP1 gene on exon-5. There was no evidence of nystagmus or strabismus. His best corrected visual acuity was 2/10 OU. His fundi were normal but for a discreet optic disc pallor temporally. Flash- and pattern-ERGs, flash- and pattern-VEPs were recorded in order to better evaluate his visual function.

Results:
Surprisingly, rod and cone ERG responses were impaired while pattern-ERG, flash- and pattern-VEPs were non-detectable.

Conclusions:
These results suggest that both the photopic and scotopic retinal systems were deficient and that macular function was also altered (no pattern-ERG). These findings point to generalized retinopathy. To our knowledge, retinopathy had not been previously described in Pelizaeus-Merzbacher disease. In fact, it is our experience that the flash-ERG in Pelizaeus-Merzbacher patients is customarily reported as normal. As retinal fibers are not myelinated, the cause for this retinopathy remains to be clarified.

Grant Support:

Keywords: Systemic Disease, Retina, YES

Financial Disclosures: The authors had no disclosures.

91 (Submitted)
Acute Compressive Optic Neuropathy Due To Spontaneous Orbital Varix Thrombosis

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Introduction:
A 76 year old woman with a prior history of right abducens palsy and Horner syndrome related to multiple sclerosis presented with acute left-sided proptosis and ptosis associated with mild pain, nausea and one episode of vomiting. She denied any recent trauma, headache or foreign body sensation. She was unaware of any change in vision at that time. An initial evaluation within hours of her presentation revealed hand motion vision and a relative afferent pupillary defect in her left eye. Acuity OS was 20/30 six months prior. There was marked ophthalmoplegia in all planes and slightly elevated intraocular pressure OS at 24 mm Hg.

Methods:
A contrast-enhanced CT Orbits revealed a large, well-circumscribed intraconal left orbital mass causing severe left-sided proptosis and mass effect on the left globe and optic nerve. There was a focal high-density material within the mass, suspicious for thrombus, and the lesion was interpreted as an orbital varix with thrombosis. CTA was consistent with the diagnosis. Conventional angiography ruled out arteriovenous fistula or aneurysm. She underwent a left lateral orbitomy and excisional biopsy of the hemorrhagic mass, which was described as benign fibroadipose tissue and blood.

Results:
Sequential exams revealed progressive improvement in extraocular motility and visual acuity. At six-month follow-up, her visual acuity was 20/60 but her visual field was markedly restricted with preservation of an inferotemporal island. The afferent pupillary defect as well as the partial third and fourth nerve palsies persisted. Her dilated exam showed pallor OS.

Conclusions:
Orbital varix thrombosis is an extremely rare complication but should be considered in the differential diagnosis of a patient presenting with acute vision loss, proptosis, and/or pain. The compressive effects of a varix thrombosis can lead to severe long-term ophthalmological morbidity. To the best of our knowledge, this is the first reported case of an acute compressive optic neuropathy due to spontaneous orbital varix thrombosis.

References:


- Khan TT, al Hariri AB. Case report: Orbital varix thrombosis following surgical prone positioning for spinal decompression. Orbit Early Online, 1–3, 2013
Introduction:
An isolated abducence nerve palsy is a rare presenting sign of nasopharyngeal carcinoma in the skull base and cavernous sinus. The authors report a case of nasopharyngeal cancer (adenoid cystic carcinoma) with intracranial extension in a patient of chronic unresolved abducens nerve palsy.

Methods:
A 52 year-old male without underlying disease was referred with abducence nerve palsy in left eye and glaucoma suspect on both eyes, which diagnosed 2 years ago with normal brain MRI. The BCVA was 20/20 on both eyes. The cup to disc ratio were 0.7 in both eyes and visual field showed inferior area defect in left eye. The fluorescein angiography demonstrated delayed arterial filling in left eye. The carotid Doppler test was normal. Patient had 25 prism diopter esotropia and wearing prism glasses. The patient wanted to take off prism glasses. We performed left medial rectus recession with adjustable suture.

Results:
After 3 months, the patient complained discomfort on left eye with 20/20 visual acuity. The visual field in his left eye showed aggravation of visual field defects involving central area. The MRI and MRA showed diffusely enhancing mass like lesion extent to skull involving orbital apex, nasopharynx and diffuse narrowing in the distal internal carotid artery. He had endoscopic transnasal approach biopsy and diagnosed with primary adenoid cystic carcinoma (ACC). He received radiation therapy for 9 months, and made recovery of visual field defect.

Conclusions:
Abducence nerve palsy may not always be due to a benign process that permits full return of function within months. Nasopharyngeal ACC must be considered in the differential diagnosis of isolated chronic sixth nerve palsy or suspicious nongranulomatous optic disc. In adults, it is essential that the nasopharynx be examined carefully in case of unexplained abducence nerve palsy.
Keywords: Cranial Nerves (Paresis etc), Posterior Afferent Visual Pathway (Post-Chiasmal), YES

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93 (Submitted)
Peduncular Hallucinosis: A lesion-based network analysis

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Introduction:
Lhermitte’s peduncular hallucinosis refers to complex visual hallucinations following a lesion of the caudal brainstem or thalamus.¹ It is hypothesized that these lesions give rise to hallucinations by engendering increased, disinhibited extrastriate visual cortex activity.²

Methods:
In order to elucidate the neural correlates of these hallucinations, we collected a series of peduncular hallucinosis cases (N=23, including twenty descriptions in the literature and three new cases) and conducted several imaging analyses. First, we employed a traditional lesion-overlap analysis to identify common lesion sites. The most common area of overlap was in the central thalamus (N=6/23), but this site did not account for a majority of cases. Next, we developed a method termed lesion-based network analysis, in which we identified the resting state functional network associated with each lesion site by querying a large resting fMRI dataset acquired from normal subjects.³ This method determines areas within a network that show functional correlation or anticorrelation during the resting state.

Results:
By identifying regions of overlap in the resting functional networks associated with each case, we demonstrated that 96% of lesions (22/23) associated with peduncular hallucinosis showed functional anticorrelation with extrastriate visual cortex.

Conclusions:
These findings demonstrate that lesion-based network analysis may represent a substantial advance in lesion-based clinical-pathologic research; in this application, the method yielded results consistent with the hypothesis that peduncular hallucinosis stems from a pathologic ‘release’ of cortical activity in visual association areas.

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References:


**Keywords:** Disorders of Vision Processing, Neuro-Imaging (MRI, CT, etc), YES

**Financial Disclosures:** The authors had no disclosures.

94 (Submitted)

**Imaging and neuroophthalmology: some clues to avoid mistakes**

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**Introduction:**
Imaging plays a mandatory part in multiple neuro ophthalmological pathologies. Both clinician and radiologists may be aware of errors leading to misdiagnosed or missed lesions and should figure out ways to avoid them.

**Methods:**
Selection of chosen cases among a four year study of neuro ophtalmological cases with a wrongly analyzed MRI, either because of poor clinical data or radiological mistakes. This presentation will propose several typical examples of both usual clinical and radiological mistakes leading to moderate or severe misdiagnosis.

**Results:**
Most common mistakes are due to both clinical and radiological sideClinician: lack of clinical information provided to the radiologist, miserable handwriting, use of complicated abbreviations often not or misunderstood by the radiologist.Radiologist: Poor knowledge of ophthalmological pathology and/or visual and oculomotor pathways, leading to inadequate imaging (wrong sequence or lack of useful sequence) or to poor reading of the images. Misreading of specific aspects of the pathology Wrong interpretation of nonspecific lesion Previous imaging not taken into account

**Conclusions:**
Clinician should always provide a detailed prescription and be critical when the patient comes back with his imaging (it fits the clinical data?? ).Radiologist should always consider clinical data while establishing the MRI protocol or reading the images. They should keep in mind that some lesions may be small, even if clinical examination shows major impairment. They should not hesitate to perform further examination or repeat the MRI in case of atypical or nonspecific images. They should remain critical, even if the diagnosis seems established. They should improve their knowledge of the pathology they have to study.Communication between clinician and radiologist before the MRI is the best weapon against misdiagnosis.

**Keywords:** Neuro-Imaging (MRI, CT, etc), Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), YES
Financial Disclosures: The authors had no disclosures.

95 (Submitted)
Ocular vascular features in mitochondrial optic neuropathies

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Introduction:
To investigate the vascular dysfunction in Leber hereditary optic neuropathy (LHON). With different techniques we evaluated: (i) vascular dysfunction in asymptomatic (cLHON), acute (aLHON) and chronic (chLHON) stages of the disease, comparing LHON patients with healthy controls; (ii) vascular setting in dominant optic atrophy (DOA), comparing DOA patients with controls.

Methods:
We investigated 6 cLHON, 2 aLHON, 8 chLHON patients and 6 DOA patients. All patients underwent a complete ophthalmologic examination including EDI-OCT (enhanced depth imaging-optical coherence tomography). Color Doppler imaging (CDI) was performed by 6 LHON patients and 4 DOA patients. Three LHON patients and 3 DOA patients ended the Retinal Vessel Analyzer exam. The healthy control groups were composed by 10 subjects for EDI-OCT and CDI and 6 subjects for RVA.

Results:
Macular choroidal thickness was significantly reduced in both aLHON and chLHON. In DOA patients we also observed a reduction of choroidal thickness reaching statistical significance only in 1500 temporal and SF measurements compared with healthy controls. The functional values obtained with CDI showed a general increase of peak systolic velocity (PSV) in aLHON and a subsequent reduction in the chronic phase of the disease.

Conclusions:
The present study revealed a structural damage of posterior vessels in LHON, probably related to the microangiopathy affecting LHON in addition to the possible non-specific correlation with the occurrence of optic atrophy, considering the reduction observed also in DOA. The result is compatible with the stroke-like hypothesis, followed by reduction of microangiopathy, once the optic nerve atrophy becomes established. The information gained by this approach will be also instrumental to assess the outcome of currently used therapies for mitochondrial optic neuropathies.

Grant Support:

Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Miscellaneous, YES

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96 (Submitted)
Integrated Visual-Auditory Perception in Amblyopic Adults: A Study Using the McGurk
Phenomenon

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Introduction:
Although classically defined as a developmental disorder characterized by a loss of visual acuity, the impact of amblyopia on multisensory integration has not been investigated previously. The McGurk effect is a perceptual phenomenon resulting from an interaction between hearing and vision in speech perception. The purpose of this study was to assess visual-auditory integration in adults with amblyopia using the McGurk effect.

Methods:
This is a prospective, single-blinded comparative study. Adults with a history of amblyopia and visually normal controls were given a background questionnaire and baseline assessment of visual acuity, stereoacuity and eye alignment. Participants were then shown a standard video of congruent (control) and incongruent (McGurk) trials consisting of various combinations of visual and auditory phonemes and asked to report what they heard.

Results:
Twenty-two adult subjects with amblyopia (19 female, mean age 32.8 years) and 25 visually normal controls (16 female, mean age 31.8 years) participated in the study. All participants performed at ceiling for congruent trials, with mean accuracy for all groups and viewing conditions exceeding 98%. With incongruent trials, people with amblyopia were significantly less likely to report hearing a fused phoneme (i.e., demonstrate the McGurk effect) compared to controls (p = 0.01). While this difference was greatest during amblyopic eye viewing, it was also present during fellow eye and binocular viewing. No correlations were found between accuracy and visual acuity or stereoacuity.

Conclusions:
This study is the first to show that adults with amblyopia have an impairment of their ability to integrate visual and auditory signals, independent of visual acuity. Visual-auditory integration is an important perceptual ability and a key component of speech perception. The results of this study add to the growing body of evidence that amblyopia causes an array of deficits beyond the visual system.

References:


**Keywords:** Disorders of Vision Processing, Posterior Afferent Visual Pathway (Post-Chiasmal), YES

**Financial Disclosures:** The authors had no disclosures.

97 (Submitted)

**Trial Design for an International Phase 2 Study of the Efficacy, Safety and Pharmacokinetics of the Anti-LINGO-1 Monoclonal Antibody, BIIB033, in Subjects With a First Episode of Acute Optic Neuritis**

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**Introduction:**
Acute optic neuritis (AON) is characterized by inflammatory injury to the optic nerve and is frequently the first manifestation of MS. In humans, ~20% of the nerve fiber layer is lost after an AON episode. LINGO-1 (leucine-rich repeats and immunoglobulin domain-containing neurite outgrowth inhibitor receptor-interacting protein-1) is a component of CNS signaling complexes that suppress axonal repair/remyelination. Blocking LINGO-1 improves remyelination in animal models, thereby providing a rationale for evaluating the anti-LINGO-1 monoclonal antibody, BIIB033 in a Phase 2 study of subjects with AON (RENEW).

**Methods:**
RENEW is being conducted at 44 centers in 11 countries in Australia, Canada and Europe to evaluate the efficacy, safety, and pharmacokinetics of BIIB033 in subjects with their first, unilateral AON episode. Eligible individuals (N=80; aged 18–55 y) are being randomized (1:1) to received intravenous infusions of BIIB033 (100 mg/kg) or placebo every 4 weeks for 20 weeks. The primary efficacy endpoint is the change in optic nerve conduction velocity at Week 24 for the affected eye from the baseline value for the unaffected eye, determined using full-field visual evoked potentials (FF-VEPs). Secondary endpoints include the change in thickness of the retinal nerve fiber layer and retinal ganglion cell layer/inner plexiform retinal layer, assessed by spectral domain optical coherence tomography and the change in low-contrast letter acuity using Sloan letter charts. Patient-reported vision-related quality of life is being measured using the 25-item National Eye Institute Visual Functioning Questionnaire. Safety and tolerability is being monitored via the incidence of adverse events (AEs) and serious AEs; population pharmacokinetics will be measured by serum concentrations of BIIB033 (ClinicalTrials.gov #NCT01721161).

**Results:**
Details of the study design for RENEW will be reported.

**Conclusions:**
RENEW is an international, Phase 2 study underway to examine the efficacy of BIIB033 in subjects with their first AON episode.

**Keywords:** Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Nerve Fiber Layer and
Retinal Testing (OCT, ERG Etc), YES

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99 (Submitted)
**Peripapillary RPE-layer shape in Idiopathic Intracranial Hypertension: before and after treatment**

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**Introduction:**
We previously reported that the shape of the peripapillary-RPE (ppRPE) layer in papilledema has an inverted U-shape indentation to mild flattening of the globe compared normals who exhibit a V-shape¹. This study attempts to determine the magnitude and type of shape changes that occur with a decrease in CSF-pressure that follows lumbar puncture and after successful treatment.

**Methods:**
We studied 30 patients with idiopathic intracranial hypertension; 27 female, mean age 25.6. We used the SD-OCT to evaluate three groups with respect to 1. shape of the RPE layer (using Geometric Morphometrics¹-⁴), 2. anterior-posterior displacement of the RPE layer at its margin and 3. RNFL thickness. We compared eyes with: A. papilledema before (Pre) and after lumbar puncture (P-lp), B. before (Pre) and after treatment with resolution (P-r); C. resolved papilledema (P-r) to normal controls.

**Results:**
There was a statistically significant difference in the shape of the RPE-layer after LP (p=.004) and after resolution (p=.001) compared to the Pre. The inverted-U indentation of the globe decreased slightly after LP and decreased further in the P-r group. Despite "resolution", the P-r shape was statistically different (p=.001) from normals. The average posterior displacement after spinal tap was -78um; and -215um after resolution. The mean RNFL at presentation was 278um, and decreased to 94um with resolution. There was a statistically significant (p=0.000) decrease of the mean RNFL (56um) after LP (before treatment). Displacement correlated with shape changes (r=.87, p=0.000). There was a statistically significant but mild correlation between displacement and RNFL change (r=.37, p=.01), shape and average RNFL (r =.44, p=.002).

**Conclusions:**
The changes in the ppRPE-shape are dynamic and presumably reflect a decrease in the intracranial pressure after LP and treatment. There is a complex relationship between the translaminar pressure, scleral compliance and structural geometry of the neural canal that affects the shape of the peripapillary eye wall⁵. Peripapillary deformations may be useful in the diagnosis and management of intracranial hypertension.

**Grant Support:**

**References:**


Keywords: CSF (Intracranial Hypertension, Intracranial Hypotension, etc), Neuro-Imaging (MRI, CT, etc), YES

Financial Disclosures: The authors had no disclosures.

100 (Submitted)
Assessment of color vision in MS using a smartphone platform

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Introduction:
Smartphone-based assessments may improve monitoring of patients with multiple sclerosis (MS).

Methods:
We designed a custom application suite consisting of 20 tests of color vision, attention, dexterity, cognition, and quality of life. We enrolled patients with MS and their cohabitating partners as control pairs. Each subject received an Android HTC Sensation 4G smartphone. During the 1-year study, subjects accessed the study application daily to complete a quasi-randomly assigned test.

Results:
43 subject pairs were enrolled. 75% of MS patients and 40% of non-MS cohabitants were female. The median age was 34.5 (range 21-52) in MS patients and 38 (range 18-55) in non-MS cohabitants. There was a 87.5% patient retention rate and 72% compliance rate. Interim analysis was performed for 38 subject pairs that completed the color vision test weekly for at least 4 months. This task requires the subject to view 9 separate pseudoisochromatic images monocularly and to type in the perceived number. Using a threshold of 8/9 correct responses, 81% of tests for MS patients and 94% of tests for controls were performed accurately. Nine MS subjects had color vision deficits in one or
both eyes. In affected eyes (n=13), the mean accuracy was 54% (SD±33.43), while the accuracy in paired controls was 99% (SD±1.46). Color vision performance modestly correlated with results from the Impact of Visual Impairment Scale.

Conclusions:
We captured high-frequency data from MS patients using a battery of assessments on a smartphone platform. Analysis of color vision test data identified eyes with poor color performance and found that those eyes demonstrated greater variance. These data illustrate the potential of smartphone-based applications to (1) gather clinically relevant data in a natural setting and (2) capture longitudinal data that may be sensitive to small but clinically meaningful changes.

Grant Support:

Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Miscellaneous, YES


101 (Submitted)
A Case of Hemi-central Retinal Artery Occlusion in 12 year-old girl

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Introduction:
Central retinal artery usually divides into two branches at the disc, each of which further bifurcates into temporal and nasal divisions. We report a case hemi-central retinal artery occlusion presumably due to bifurcation of central retinal artery behind the lamina cribrosa.

Methods:
A 12-year-old girl with 6 months of history of decreased visual acuity visited our clinic. She was taking medication for vitamin D deficiency. She had a history of syncope and spinning sensation. Her tests performed by otolaryngologist were normal. On examinations her corrected visual acuity was 20/50 in each eye. Both anterior segments were normal. On fundus examinations superior and inferior hemi-trunks of central retinal artery were emerging separately in both eyes. We performed multifocal-ERG, visual field test, macular OCT and FAG.

Results:
Both eyes showed decreased amplitude in multifocal-ERG, macular thinning in OCT and visual field constriction in Humphrey visual field (central 30-2). In FAG, inferior branch of retinal artery of right eye showed delayed filling as 20/50 in each eye. Both anterior segments were normal. On fundus examinations superior and inferior hemi-trunks of central retinal artery were emerging separately in both eyes. We performed multifocal-ERG, visual field test, macular OCT and FAG.

Conclusions:
On entering the eye, central retinal artery loses the elastic lamina and has a prominent muscularis as it bifurcates at the optic disc. Unusual bifurcation of central retinal artery behind the lamina cribrosa coupled with the unique histological features of the retinal arterioles (hemi-trunks) may predispose to the development of ‘hemi-central retinal artery occlusion’ in young patients.
Introduction:
Ophthalmologists face an ethical dilemma when communicating with patients diagnosed with non-organic vision loss (NOVL) – should they reveal the findings of the exam and diagnosis of NOVL risking an angry breakdown in trust; or should they offer something more acceptable to the patient, avoiding discussion of psychiatry or suspicions of pretending? This dilemma reflects the ethical obligation of physicians to weigh the principle of respect for autonomy against the principle of beneficence. We conducted an international survey of neuro-ophthalmologists to examine professional perspectives regarding diagnosis and management of NOVL for adults and children with the goal of promoting discussion of the ethical implications for clinical practice.

Methods:
All members of the North American Neuro-Ophthalmology Society listserv were surveyed with 240/500 responding (48%).

Results:
Using deceptive methods to prove visual acuity was viewed as ethically appropriate (99.2%). Confrontation involving the disclosure of a NOVL diagnosis was not favored in adults (11.4%) and children (4.9%) without a perceived secondary gain. In contrast, confrontation was favored in adults with a perceived secondary gain (49.2%). Treatment of children with a placebo (3.8%) was favored more highly than placebo treatment of adults (1.6%).

Conclusions:
Ophthalmologists adapt their disclosure of diagnoses and treatment to their patients, which imposes some limits on truth-telling. The best method for communicating the diagnosis of NOVL will need to balance ethical considerations with therapeutic benefit. When the therapeutic benefit of deception is unproven, physicians have a duty to disclose.

Keywords: Disorders of Vision Processing, Miscellaneous, YES

Financial Disclosures: The authors had no disclosures.
Introduction:
Learning direct ophthalmoscopy is challenging, and medical students’ (MS) long-term retention of ophthalmoscopy skills is poor.\textsuperscript{1} We previously demonstrated that MS performed more accurately and preferred using photographs than direct ophthalmoscopy to examine the ocular fundus.\textsuperscript{2} We hypothesized that these differences would persist over time.

Methods:
One year after initial training, second-year MS were randomized and reevaluated on their ability to examine the ocular fundus using either fundus photographs or direct ophthalmoscopy on eye simulators.\textsuperscript{3} Positive and negative affect, preferences, and clinical experiences with ocular fundus examination were assessed.

Results:
107/119 students (90%) who participated in the original study completed this one-year retention study. Students answered 34/48 (71\%) questions correctly using photographs and 31/48 (65\%) correctly using ophthalmoscopy (p<.01). Both photograph and ophthalmoscopy groups answered five fewer questions correctly on average than one year prior (p<.001). Students rated photographs as “easier than ophthalmoscopy” (8/10 vs. 6/10, respectively; p<.001). Students’ positive affect scores were higher in the photograph group (26.5) than in the ophthalmoscopy group (23.2; p=.03). Students tested on simulators reported lower positive affect than one year ago (decrease of 6.4 points, p=0.001). Students' self-reported median frequency of fundus examination over the preceding year was <10\% (IQR 0-20\%). Ocular fundus examination was not performed because of discomfort with the examination (38\%), discouragement by their preceptor (20\%), and insufficient time (15\%). 79\% of students felt uncomfortable with ophthalmoscopy, and 44\% stated that they would not perform ophthalmoscopy during a general physical examination. 76\% stated they would prefer using photographs instead of ophthalmoscopy for fundus examination.

Conclusions:
Students preferred photographs for examining the ocular fundus and were more accurate using photographs vs. direct ophthalmoscopy one year after training. The increasing availability of non-mydriatic ocular fundus photography may allow more frequent and accurate examination of the ocular fundus by MS and non-ophthalmologists in many clinical settings.

References:

Keywords: Miscellaneous, Miscellaneous, YES
Introduction:
Truly asymmetric papilledema in IIH is rare and poorly characterized. Our goal was to determine the prevalence and the clinical and radiologic features of IIH with highly asymmetric papilledema.

Methods:
Retrospective review of all definite IIH patients seen by us between 1989 and 2013. Papilledema was graded (modified Frisén scale) by reviewing fundus photographs. Asymmetric papilledema was defined as ≥2 grades difference between the 2 eyes. Clinical and radiologic characteristics were reviewed.

Results:
Of 725 IIH patients, 18 (2.5%) had ≥2 grades difference papilledema between the 2 eyes at initial evaluation [age: 38±11 year-old; 15 women (83%); 11 white (65%); 6 black (35%); all overweight (BMI=43.7±20.3kg/m²); 3 with sleep apnea, 2 taking vitamin A-derived medications, 1 with anemia]. CSF opening pressure was 32.2±9.0cm H₂O. 11/18 patients (61%) had the highest-grade edema in the left eye; papilledema was unilateral in 8 patients (44.5%). 6/18 patients (33%) presented with isolated transient visual obscurations (TVOs) and 6/18 patients (33%) were asymptomatic. Brain imaging (6 MRI, 1 CT), was available for review in 7 patients. Optic canal measurement showed larger area cross-section on the side of the highest-grade edema by 3.4±3.6mm² for all 3 patients in whom this technique was available. 4/7 patients (57%) showed prominent peri-optic nerve CSF; it was always greatest on the side of the highest-grade edema. There was no relationship between the side of the highest transverse venous stenosis and the side of the highest-grade edema.

Conclusions:
Asymmetric papilledema is rare in IIH. Clinical presentation differs from classic IIH by the frequency of isolated TVOs at presentation, and of asymptomatic IIH. Asymmetric edema may originate from difference in size of both optic canals, with the larger canal allowing CSF pressure to be transmitted more easily to the optic disc, which may explain the prominent peri-optic CSF on the side of the high-grade edema.

References:

Keywords: CSF (Intracranial Hypertension, Intracranial Hypotension, etc), Neuro-Imaging (MRI, CT, etc), YES
Introduction:
While several large cohort studies have associated ocular fundus abnormalities with the long-term risk of stroke, the value of ocular fundus examination in patients presenting with focal neurologic deficits, particularly suspected transient ischemic attack (TIA) and stroke, has not been evaluated. The ABCD2 score is widely used for the risk stratification of patients with suspected TIA, but does not include fundus findings. Our objective was to determine the frequency of and the predictive factors for abnormal ocular fundus findings among ED patients who presented with focal neurologic deficits.

Methods:
Cross-sectional study of prospectively enrolled adult patients presenting to our ED with a chief complaint of focal neurological deficits. Ocular fundus photographs were obtained using a non-mydriatic fundus camera. Demographic and neuro-imaging information were collected, including the ABCD2 score components. Two neuro-ophthalmologists independently reviewed photographs for acute retinopathic/vasculopathic findings (i.e., retinal hemorrhages, cotton wool spots, grade III/IV hypertensive retinopathy, and retinal vascular occlusions). The results were analyzed using univariate statistics and logistic regression modeling.

Results:
We included 257 patients (median age: 52 years, 63% women), among whom 81 (32%) had cerebrovascular disease (CVD; 22 strokes, 59 TIs) and 17 (7%; 95%CI: 4-11%) had acute retinopathic/vasculopathic findings. Acute retinopathic/vasculopathic findings were associated with CVD among patients with focal neurologic deficits (odds ratio [OR]=3.4; 95%CI: 1.2-9.3; p=0.02), and a trend toward association remained after controlling for ABCD2 score and abnormal diffusion weighted imaging (DWI; OR=2.5; 95%CI: 0.8-7.2; p=0.10).

Conclusions:
Ocular fundus abnormalities were found in 7% of patients presenting with focal neurologic defects to our ED, and predicted CVD among these patients, probably even after accounting for ABCD2 score and DWI lesions. This suggests that inclusion of non-mydriatic ocular fundus photographs in the evaluation of patients with focal neurologic deficits could assist in the differentiation of high-risk CVD from other causes of focal neurologic deficits and warrants additional study.

Keywords: Miscellaneous, Systemic Disease, YES

Financial Disclosures: The authors had no disclosures.
Persistent Positive Visual Phenomena Revisited

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Introduction:
Patients occasionally report persistent positive visual phenomena (PPVP) with features that differ from those typically associated with visual migraine. Often, such PPVP are described, or can be interpreted, as being consistent with “visual snow.” We report a series of patients with PPVP and “visual snow” that provides additional clinical commentary of the visual and clinical features of this disorder.

Methods:
A retrospective analysis of all patients who presented to a single Neuro-Ophthalmologist from 2009-2013 with “visual snow” was performed. The charts coded with the diagnosis of “visual snow” were reviewed for information in regard to 17 features of the medical history and visual presentation. All patients were interviewed by telephone to clarify the details of our chart review.

Results:
A total of 20 patients with “visual snow” were identified. The majority of patients reported visual symptoms only of “visual snow.” In all cases, the qualitative descriptions were remarkably similar, nearly stereotypical. No patient with isolated “visual snow” experienced disruption of function. MRI scans of all patients were normal. No patient had evidence of neurological disease. Anxiety and depression were present in a minority of patients. Most patients’ symptoms persisted without significant variation for months to years. No treatment attempted by any patient seemed to be effective. A minority of patients reported visual symptoms in addition to the visual snow. Many patients had a history of migraine.

Conclusions:
PPVP with features of “visual snow” is a benign phenomenon that does not require diagnostic investigation or medical intervention. The etiology of visual snow is not known, and migraine remains a plausible factor. The fact that the spontaneous description of visual snow is so stereotypical strongly suggests that it is caused by some biological perturbation, and is not simply a reaction secondary to psychological factors, as is sometimes suggested.

Keywords: Disorders of Vision Processing, Miscellaneous, YES

Financial Disclosures: The authors had no disclosures.

Rare Primary Central Nervous System Melanoma

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Introduction: Melanocytes arise from neural crest cells and are prevalent in the skin. However, melanocytes are also present in other neural crest derivatives, including heart, bowel, bone marrow, mucous membranes, uveal tract, and leptomeninges. Although melanoma usually originates in the skin, it is possible to have a melanoma originate from these other locations.

Methods: A 59 year-old man reports blurry vision, reduced peripheral vision, and difficulty reading for the past 3 months. He has a 2-year history of ocular migraines with aura, which occur after exercise. He has been having worsening headaches over the past month, one of which awoke him from sleep. Examination is remarkable for a congruous right inferior homonymous hemianopia.

Results: MRI reveals a mixed cystic and solid mass in the left occipital lobe, most consistent with a glioblastoma, for which the patient undergoes prompt neuro-surgical removal. Unexpectedly, biopsy shows that this is not a glioblastoma, but rather a melanoma. Thorough work-up shows no other primary site of involvement to indicate a metastatic melanoma. Therefore, a diagnosis of primary CNS melanoma is made.

Conclusions: Primary CNS melanoma is a rare malignant tumor arising from the melanocytes in the leptomeninges of brain or spinal cord, and accounting for only 1% of all melanomas. Primary CNS melanoma can appear similar to astrocytoma and glioblastoma on imaging, as demonstrated in this case. It is not possible to distinguish a primary CNS melanoma from a secondary metastatic melanoma based on either imaging or histopathology.

Keywords: Posterior Afferent Visual Pathway (Post-Chiasmal), Neuro-Imaging (MRI, CT, etc), YES

Financial Disclosures: The authors had no disclosures.

111 (Submitted)
An Unusual Presentation After Blunt Orbitocranial Trauma

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Introduction: Traumatic cerebrospinal fluid (CSF) leak usually manifests as otorrhea or rhinorrhea. Rarely CSF may also leak into the orbit manifesting tearing (“oculorrhea”) [1-5]. We report an additional case, the first to be documented by beta-transferrin testing of subconjunctival fluid.

Methods: A 34 year old policeman struck by a car developed orbito-cranial fractures. The marked conjunctival chemosis was puzzling until copious tearing appeared upon leaning the patient’s head forward.

Results: Needle aspiration of subconjunctival fluid was positive for beta 2-transferrin, a specific marker for CSF. Without intervention, oculorrhea ceased within 6 days.

Conclusions:
Oculorrhea is a rare manifestation of orbitocranial fracture. It may be overlooked in the chemotic orbital tissues. Prompt recognition is critical because meningitis, reported in 2 cases (2,5) is a threat. Diagnosis may be confirmed by testing needle aspirate of subconjunctival fluid for beta-transferrin positivity.

References:

Keywords: Orbital and Eyelid Disorders, CSF (Intracranial Hypertension, Intracranial Hypotension, etc), YES

Financial Disclosures: The authors had no disclosures.

112 (Submitted)
A Non-Touch Slit-Lamp Exophthalmometry, A Novel Technique

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Introduction:
Exophthalmometry is frequently used in neuro-ophthalmogy practice. We describe a novel non touch exophthalmometry technique performed with the basic ophthalmology slit lamp device, and compare the measurements results with those of the Hertel exophthalmometer

Methods:
A millimeteric graph paper covered by transparency is attached to the slit-lamp table. The slit-lamp is first focused on the center of the cornea and the position of the microscope is marked on the transparency, then the slit lamp is focused on the lateral orbital rim and a second mark is drown. The distance between the two lines as measured on the graph paper represents the exophthalmometry score. 60 patients with suspected orbital disease underwent both slit-lamp and Hertel exophthalmometry and the results were compared.

Results:
Exophthalmometry mean results for the right eye were 19.8±3.3 mm with the slit lamp and 19.5±3.4 with the Hertel. Mean measurements for the left eye were 19.3±4 mm with the slit lamp and 19.6±3.8 with the Hertel. t test for paired samples did not show statistically significant difference in the
measurements between the two methods. In only 6 out of 120 measurements there was more than 2 mm of difference between the two techniques.

**Conclusions:**
Slit lamp exophthalmometry is a reliable non-touch technique which does not require the use of an exophthalmometer.

**Keywords:** Orbital and Eyelid Disorders, Miscellaneous, YES

**Financial Disclosures:** The authors had no disclosures.

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114 (Submitted)
Investigating Regional Grey Matter as Well as White Matter Atrophy in MS Retinal Nerve Fiber Layer Thickness and Thalamus Pathology in Multiple Sclerosis Patients

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**Introduction:**
Multiple Sclerosis is commonly categorized as an inflammatory disease of the brain’s white matter. Studies have been conducted measuring RNFL loss in MS, but newer studies are relating levels of RNFL loss to regional brain atrophy of the white as well as the grey matter of the CNS. Our research indicates early grey matter involvement in MS. This is important to ascertain since it is known that grey matter damage is a critical factor leading to permanent disability in this disease.

**Methods:**
RNFLT was measured using OCT in 96 relapsing-remitting MS (RR-MS) patients (41% had history of optic neuritis), 25 secondary-progressive MS (SP-MS) patients (40% had a history of optic neuritis) and 46 controls. MRI was obtained within ± 3 months of OCT testing. RNFLT associations with MRI by diffusion tensor imaging were assessed in regression analyses.

**Results:**
In RR-MS, lower RNFLT was associated with lower white matter (WM) volume and lower whole brain volume. In RR-MS, lower RNFLT was associated with lower total deep gray matter (GM) volume and lower thalamus volume. In RR-MS, lower RNFLT was associated with greater mean diffusivity (MD) in normal appearing brain tissue (NABT) and NAGM. Trends were found for lower RNFLT with greater MD in NAWM and thalamus. RNFLT in controls and SP-MS was not associated with MD in NABT, NAGM, NAWM and in the deep gray matter, thalamus or pulvinar regions.

**Conclusions:**
Lower RNFLT is associated with MRI metrics of microscopic tissue injury in normal appearing (NA) regions of the brain. RNFLT is associated with, and could potentially be an imaging biomarker for, neurodegeneration of the deep gray matter and thalamus in RR-MS.

**References:**


**Keywords:** Posterior Afferent Visual Pathway (Post-Chiasmal), Neuro-Imaging (MRI, CT, etc), YES

**Financial Disclosures:** The authors had no disclosures.

116 (Submitted)
**Eye on the Ball: A Case Report**

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**Introduction:**
We report an unusual presentation of a patient with orbital apex syndrome caused by invasive fungal sinusitis

**Methods:**
Single case referred to a tertiary-level academic center

**Results:**
A 73 year old woman was seen by the ophthalmology consultation service for progressive vision loss, ptosis, and decreased eye movements in the left eye. Past medical history was significant for rheumatoid arthritis on extensive iatrogenic immunosuppression. Examination was concerning for left optic neuropathy with no light perception vision associated with 3rd, 6th, and V1 cranial nerve deficits. The patient’s initial neuroimaging was reviewed and was concerning for subtle enhancement of the left posterior sphenoid sinus. Initial sinus endoscopic examination was unremarkable. Given the patient’s lack of improvement on broad spectrum antibiotics and antiinflammatories, neuroimaging was repeated and revealed worsening left posterior sphenoid sinus sinus involving the left orbital apex. The patient was taken to the operating room and a large necrotic collection was removed from the sphenoid sinus. Pathology revealed numerous invasive septate hyphae consistent with Aspergillus infection. The patient was started on antifungals systemically and immunosuppression was titrated lower. Unfortunately the patient’s respiratory status decompensated and she expired one week after diagnosis.

**Conclusions:**
Fungal disease should always be included in the differential diagnosis of orbital apex disease, especially in the immunocompromised patient. Invasive fungal sinusitis carries an extremely high mortality. Successful treatment depends on early diagnosis, institution of antifungals, and careful titrating of immunosuppression as tolerated.

**Keywords:** Orbital and Eyelid Disorders, Cranial Nerves (Paresis etc), YES

**Financial Disclosures:** The authors had no disclosures.
Introduction:

Methods:
A retrospective multi-center chart review identified children (4-17 years) diagnosed with IIH from 2002-2012. Gender, age, body mass index (BMI), opening pressure, optic nerve head (ONH) edema, treatment and outcomes were identified.

Results:
Fifty-four patients were divided into group 1 (4-8 years), group 2 (9-12 years) and group 3 (13-17 years). The average age was 11.5 years, differing significantly between males and females (9.7 versus 13.3 years, p=0.001). Females represented 67% of all patients (26/54) and 86% of patients in group 3 (18/21). Group 2 represented the most patients overall (23/54), split evenly between males and females (52% versus 48%, respectively). ONH edema was most severe in group 3 and higher in females (median grade 4). The average opening pressure was 45mm water, highest in females (55) and in group 2 (42.8), and lowest in group 1 (30.9). Medical treatment was the predominant management method (41/54), of which 63.4% were female (26/41). In the medical group, the average ONH edema was grade 2 (p=0.04) with median visual acuity of 20/25 pre-intervention and 20/20 post-intervention. ONH edema post-intervention revealed a median of grade 0. Thirteen children underwent surgical intervention, of which 70% were female (9/13). In the surgical group, the average grade of ONH edema was grade 3 (p=0.04) with median visual acuity of 20/70 pre-intervention and 20/25 post-intervention. The median ONH edema post-intervention in the surgical group was grade 1. The recurrence rate was 13%.

Conclusions:
The epidemiology of IIH differs in children and is age-dependent. Although both treatment groups demonstrated improvement in vision and ONH edema, outcomes were worse in the surgical group. Pubescent female patients require more invasive treatment methods and have worse visual prognosis.

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**Keywords:** CSF (Intracranial Hypertension, Intracranial Hypotension, etc), Systemic Disease, YES

**Financial Disclosures:** The authors had no disclosures.

**118 (Submitted)**

Familial Neuromyelitis Optica in a Mother and Daughter: Case and Literature Review

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**Introduction:**

We describe cases of anti-aquaporin (AQP)-4 antibody-positive neuromyelitis optica in a mother and daughter, which is the second instance to our knowledge of a child manifesting the disease prior to the parent.

**Methods:**

Retrospective chart review and literature review.

**Results:**

A woman with onset of transverse myelitis at age 38 was eventually found to have a positive anti-AQP-4 antibody during work-up of recurrent symptoms. Subsequently she developed intermittent
episodes of monocular vision loss with optic nerve involvement that were treated with IV solumedrol and Rituxan. Eighteen years after initial presentation, her 78-year-old mother with a history of recurrent urinary tract infections also developed monocular vision loss and the anti-AQP-4 antibody was positive. Although disease onset took place at different ages in the mother and daughter, the shared genetic lineage suggests a familial contribution to NMO and highlights the importance of family history during clinical evaluation.

Conclusions:
Genetic influence in the development of NMO is suggested by this family and several prior reports of familial NMO.

Keywords: Systemic Disease, Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), YES

Financial Disclosures: The authors had no disclosures.

121 (Submitted)
HE3286 Suppression of Experimental Optic Neuritis

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

Methods:
EAE was induced in C57/Bl6 mice by immunization with myelin oligodendroglial glycoprotein peptide. Mice were treated daily with vehicle or 40 mg/kg HE3286 i.p. Visual function was assessed by optokinetic responses (OKR) at baseline and every 10 days until sacrifice 6 weeks post-immunization. Retinas and optic nerves were isolated. Inflammation was assessed by H&E staining, and demyelination was assessed by luxol fast blue staining of optic nerve sections. Retinal ganglion cells (RGCs) were immunolabeled with Brn3a antibodies to quantify RGC survival.

Results:
Progressive decreases in OKR occurred in vehicle-treated EAE mice, and HE3286 treatment significantly reduced the level of this vision loss. HE3286 also significantly attenuated the degree of inflammation and level of demyelination in EAE optic nerves as compared to nerves from vehicle-treated EAE mice. RGC loss was observed in eyes from both vehicle- and HE3286-treated EAE mice, with a trend toward increased RGC survival in the HE3286-treated mice.
Conclusions:
HE3286 suppresses inflammation and reduces demyelination during experimental optic neuritis, although neuroprotective effects of this treatment may be limited. Importantly, HE3286 treatment also preserves some RGC function. Results suggest HE3286 is a potential novel treatment for optic neuritis and MS that warrants further study.

Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Systemic Disease, YES

Financial Disclosures: Co-author Clarence Ahlem is a full-time employee of Harbor Therapeutics, INC., the company that produces the HE3286 compound that was tested in the preclinical animal studies in this abstract.

Cataract Morphology Detected by Schiempflug Anterior Segment Analysis in Subjects with Pre-Clinical Alzheimer Dementia

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Introduction:
Conflicting reports exist describing the presence of β-amyloid and distribution of lens opacification in post-mortem cataracts in patients with Alzheimer disease [1, 2]. The purpose of this study was to quantitatively examine the morphology of cataracts in individuals with and without positive molecular biomarkers for Alzheimer disease (AD).

Methods:
Patients enrolled into the study were either AD biomarker positive or negative, with the former group at high risk for progression to cognitive impairment [3]. Biomarker positive individuals demonstrated amyloid-β (Aβ) in the cerebrospinal fluid (CSF Aβ₄₂ > 440 pg/ml) and/or elevated Pittsburgh compound B (Pib) on positron emission tomography (PET) Aβ fibrillar imaging. Patients received an extended clinical and neuropsychological assessment to determine the presence of cognitive impairment. All patients underwent Scheimpflug anterior segment slit lamp photography. Scheimpflug biometric analysis, performed by investigators masked to biomarker status, was used to objectively quantify the thickness and density of the cortical and nuclear portion of the lens. Statistical analysis was performed to determine whether any significant difference in lens morphology existed between the CSF Aβ and Pib imaging biomarker positive and negative groups.

Results:
33 patients were enrolled, of whom 12 demonstrated positive biomarkers for Aβ by PET imaging or CSF analysis. 10 Aβ biomarker positive individuals did not show any evidence of cognitive impairment at the time of exam. Scheimpflug lens analysis demonstrated that no significant difference existed between the Aβ biomarker positive and negative groups in mean anterior-posterior thickness of the nuclear or cortical lens portions (P = 0.600, P= 0.125 respectively). Similarly, no significant difference was found between the Aβ biomarker positive and negative groups in nuclear or cortical lens opacification (P = 0.974, P= 0.453 respectively).

Conclusions:
Our results suggest that lens morphology in Alzheimer’s patients is non-specific, and may not be a useful biomarker predicting development of cognitive impairment in Alzheimer disease.

References:

Keywords: Systemic Disease, Nerve Fiber Layer and Retinal Testing (OCT, ERG Etc), YES

Financial Disclosures: The authors had no disclosures.

124 (Submitted)
Iatrogenic ophthalmic artery occlusion caused by collagen injection during cosmetic procedure

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Introduction:
We presented an acute ophthalmic artery occlusion caused by facial filter injection during comic procedure in a small beauty salon near Shanghai city, China.

Methods:
case report

Results:
A 37-year-old woman presented with blindness and painful ophthalmoplegia in the right eye after collagen injection on her right nasolabial while doing rhinoplasty. The neuro-ophthalmology examination 28 hours later revealed the patient to be alert and oriented. Best corrected visual acuities were no light perception OD and 20/20 OS. Pupils were 5mm OD and 3mm OS and showed no direct or consensual light response OD, whereas a reversed relative afferent pupillary defect in the left eye. The lid showed 3 mm ptosis on the right. Examination of extraocular motility revealed ophthalmoplegia in all directions OD (Fig 1). Slit lamp examination revealed normal conjunctiva, cornea, anterior chamber. The crystalline lenses were normal. Applanation tonometry revealed pressures of 8 mm Hg OD; 12 mm Hg OS. Funduscopic examination revealed severe diffuse edema of the retina, as well as the optic nerve OD without a cherry red spot in macular (Fig 2). Spectral-domain optical coherence tomography (SD-OCT) showed decreased vascularity in the choriocapillaris and large choroidal vessels with edema of the macular and peripheral retina. Orbital MRI showed the acute ischemic of the right optic nerve, the ocular muscles and lacuna lesions in...
Conclusions:
Facial cosmetic injections caused acute ophthalmic artery and/or retina artery embolism had been reported mostly in Korea and the vision loss is profound when emboli retrograde to the more proximal artery--ophthalmic artery. Although some precautions may minimize the risk of embolization, plastic surgeons and patients should be aware of the dangerous of blindness while injecting filter for facial cosmetic procedure.

References:

- References

Keywords: Retina, Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), YES

Financial Disclosures: The authors had no disclosures.

126 (Submitted)
Intravenously Administered Neostigmine Combined with Prism and Alternate Cover Test as a Diagnostic Test for Myasthenia Gravis with ocular involvement

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Introduction:
To address the validity of intravenous neostigmine administration combined with prism and alternate cover test (PACT) as a confirmatory diagnostic method for confusing cases of myasthenia gravis with ocular involvement.

Methods:
Neostigmine was administered intravenously in ten suspicious myasthenic diplopia patients under electrocardiographic monitoring. Distance deviation at primary position was evaluated with PACT at 5, 10, 15, 20 and 30 minutes after intravenous injection of neostigmine. Lid position and range of duction were also evaluated at each time points.

Results:
Six out of 10 patients were diagnosed as myasthenic diplopia by positive neostigmine test. Among these patients, everyone had abnormal ocular motility and 4 had ptosis. In participants who showed positive result, impairment of ocular motility was relieved invariably, but ptosis was not improved in one patient. The improvement of ocular motility had been occurred within 5 minutes in all 6 responders and the pharmacological effect reached peak at 5 to 20 minutes after neostigmine
Conclusions:
Intravenous neostigmine administration combined with PACT is a rapid, objective and quantifiable method in hard-to-diagnose cases of myasthenia gravis with ocular involvement. In performing neostigmine test for myasthenia gravis with ocular involvement, not only the lid position, but also ocular motility should be evaluated quantitatively to avoid a false negative result.

Keywords: Misc Motility Disorders (Nystagmus etc), Miscellaneous, YES

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127 (Submitted)
Understanding Optic Neuritis from Murine Models of Multiple Sclerosis

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Introduction:
The availability of a good animal model is critical for understanding MS and developing therapies to control the disease. The primary experimental MS animal model has been the experimental autoimmune encephalomyelitis (EAE) model. Another model of viral induced CNS demyelination was recently published, based on ocular infection with a recombinant HSV-1 constitutively expressing murine IL-2 (HSV-IL-2).

Methods:
Study design: experimental animal research approved by IACUC committee. We used six-week old female C57BL/6 mice and compared MOG35–55, MBP35–47, and PLP190–209 models of EAE with our viral-induced MS model, using clinical and hysto-pathologic data to assess demyelination (LFB), inflammation (HE) and immune cells infiltration (FACS). We also looked at the possibility of blocking optic nerve (ON) demyelination using IFN-β, IL-4 and IL-12p70.

Results:
Mice ocularly infected with HSV-IL-2 showed a significant delay of VEPs compared with mice infected with control viruses. Mice with viral-induced and MOG-induced inflammatory demyelinating disease demonstrated similar pattern and distributions of demyelination in their ON, brain and spinal cord. In contrast, no demyelination was detected in ON of MBP- and PLP-injected mice. Inflammatory score in ON of MOG group was significantly higher than PLP, MBP and HSV-IL-2 groups. Except for ON in MOG group, inflammatory responses did not correlate with severity of demyelination. Mice injected with IFN-β DNA showed no ON demyelination in both MOG and HSV-IL-2 models. While HSV-IL-12p70 protected HSV-IL-2 infected mice from optic neuritis, ON demyelination, clinical severity and mortality increased in MOG group infected with HSV-IL-12p70.

Conclusions:
HSV-IL-2 ocularly infected mice behave like MOG-injected in terms of optic neuritis and MS clinical and pathological characteristics. In MBP and PLP animal models of MS, ON demyelination was not histo-pathologically described. Therefore, MOG and HSV-IL-2 models are better animal models for studying ON demyelination.
Cyanocobalamin is a Superoxide Anion Scavenger and Neuroprotectant in Neuronal Cells

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Introduction:
Vitamin B₁₂ deficiency can cause an optic neuropathy characterized by bilateral centrocecal scotomas. The mechanism for this is not well understood. In 2009, another group demonstrated that vitamin B₁₂ scavenges superoxide as effectively as superoxide dismutase (SOD). Our prior work showed that retinal ganglion cells (RGC) axotomy induced a burst of superoxide that then led to RGC death. We hypothesized that superoxide scavenging by cyanocobalamin, the most abundant vitamin B₁₂ vitamer, would be neuroprotective, and studied this in vitro and in vivo.

Methods:
Superoxide reacts with hydroethidine to produce a fluorescent product, 2-hydroxyethidium. Superoxide scavenging by cyanocobalamin in a cell-free system was measured with a fluorescent microplate reader. Superoxide scavenging in 661W cells was assessed in vitro by fluorescent microscopy. Neuroprotection against menadione was evaluated by calcein-AM/propidium iodide assay. An optic nerve transection model in Long-Evans rats was used to study superoxide scavenging and neuroprotection in vivo, with visualization of retrograde-labelled RGCs by confocal scanning laser ophthalmoscopy.

Results:
Cyanocobalamin at concentrations of 10 μM and 100 μM reduced the rate of superoxide generation by 34% and 79% in cell-free assays. In menadione-treated 661W cells, cyanocobalamin concentrations above 10 nM scavenged superoxide anion similar to cells treated with pegylated-SOD. Cyanocobalamin at concentrations of 100 μM and 1 mM reduced 661W cell death from menadione by 20% and 32%, respectively. In rats with unilateral optic nerve transection, a single intravitreal dose of 667 μM cyanocobalamin significantly reduced the number of 2-hydroxyethidium–positive RGCs and also increased RGC survival.

Conclusions:
These data suggest that vitamin B₁₂ may be an endogenous neuroprotectant, which could cause RGC death by a superoxide-dependent mechanism when depleted in nutritional deficiency. Vitamin B₁₂ could potentially be used to slow progression of RGC death in patients with optic neuropathies characterized by overproduction of superoxide.

Keywords: Anterior Afferent Visual Pathway (Optic Neuropathy and Chiasm), Systemic Disease, YES
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129 (Submitted)
Isolated Horizontal EOM deficits in a patient with Platybasia

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Introduction:
Anomalies of the hindbrain, posterior fossa, and skull base can cause visual symptoms due to their effects on oculomotor pathways in the brainstem and cerebellum. Anomalies at the craniocervical junction, such as Chiari malformations, often cause downbeating nystagmus. We have not found a previous report of isolated horizontal gaze deficits in the setting of anatomic variants affecting the craniocervical junction.

Methods:
A 67 year old man was referred to our clinic for evaluation of horizontal nystagmus, found during Neurology consultation for blurred vision, gait problems, and “head pressure” in the occiput. He had problems following fast-moving objects even as a young man, but this worsened over the years. He had worsening gait imbalance over the years, resulting in frequent falls. He had history of hypertension and hyperlipidemia. He was not diabetic, did not abuse alcohol or smoke. On exam, his mentation and speech were normal. He had normal acuity, color vision, and visual fields. Pupils were 7 mm and briskly reactive. He had normal optic discs, vessels, and maculae. He had normal vertical saccades and pursuits. No eye deviations were found on cover-uncover or cross-cover tests. Horizontal pursuit movements were absent, only saccades were seen. He had normal horizontal VOR responses, but no VOR cancellation. No horizontal optokinetic responses were elicited. Gaze-paretic horizontal nystagmus was present on extremes of gaze. On neurologic exam, he had positive Romberg, wide-based gait, and poor postural stability. MRI brain imaging a year earlier had revealed variant cranio-vertebral junction anatomy suggesting platybasia, resulting in increased angulation at the cervico-medullary junction. A relatively small posterior fossa was seen, and mildly low lying peg-shaped tonsils were noted.

Results:
Eye movement recordings to further characterize the oculomotor deficits are planned for the near future.

Conclusions:
Posterior fossa anomalies affecting the craniocervical junction can result in isolated horizontal EOM dysfunction.

References:
130 (Submitted)
Immunologic Biomarkers of Ocular Myasthenia Gravis in Children

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Introduction:
Pediatric onset myasthenia gravis (MG) is profoundly understudied and development of novel therapeutics is compromised by the lack of biomarkers. The immunologic profile of children with ocular (OMG) has not been investigated. The purpose of this study was to determine the IgG subclass and cytokine profiles of pediatric patients with OMG and compare them to generalized (GMG) forms of MG and controls.

Methods:
 Eleven children with MG (9 OMG, 2 GMG) and 4 control subjects provided serum samples. MG subjects had a mean age of 9.1 years (range 3.9 – 15.6) and a mean duration of symptoms of 3.2 years (range 0.16 – 6.3 years). Two subjects were on prednisone for less than 6 months. Acetylcholine receptor (AChR) specific IgG and subclass titers were determined by ELISA. Cytokine profiles were analyzed by Human Cytokine Array Panel A from R&D Systems.

Results:
All symptomatic OMG subjects (8 of 9) and GMG subjects demonstrated elevated AChR-IgG and AChR-IgG subclasses compared to control sera. GMG subjects had higher IgG titers and higher levels of granulocyte macrophage colony-stimulating factor (GM-CSF), chemokine (C-C motif) ligand 1 (CCL1), IL-1ra, CXCL10 and IL-17E compared to OMG subjects. All OMG and 1 GMG subject demonstrated reduction in C5/C5a complement levels. Total complement activity (CH50) was markedly reduced in all cases of symptomatic OMG.

Conclusions:
Pediatric OMG subjects have a unique immunologic profile whose cytokine levels suggest several potential points of immune system deregulation. Preferential involvement of extraocular muscles in OMG indicates a reduction of intrinsic complement inhibitors (Kaminski, 2004). Our findings suggest that future therapeutics for pediatric OMG could potentially include complement inhibitors.

References:

Keywords: Orbital and Eyelid Disorders, Systemic Disease, YES

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