ABSTRACTS

Neuro-Ophthalmic Literature Review

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THE RAREBIT DIGIT TEST—A QUICK AND ACCURATE WAY TO ASSESS NEUROVISUAL INTEGRITY?

Frisén L. Rapid assessment of neurovisual integrity using multiple rarebits. *Ophthalmology* 2013;120:1756–1760.

Central visual acuity measurement is usually the primary test of vision, but when used alone, it may not correlate well with neurovisual dysfunction. Complete assessment of visual function usually requires testing additional aspects, e.g., colour vision, contrast sensitivity, and visual fields, which is time-consuming. In this study, the author proposed a new rapid screening test for visual dysfunction, the rarebit digit test (RDT). Rarebits are receptive field-sized bright dots briefly presented on a dark background (not to be confused with the dish of melted cheese on toast, as in Welsh rarebit). In the RDT, a computer-based test, segmented digits defined by rarebits were presented to the subjects over 8 seconds and the subjects had to read as many digits as possible (maximum 6 digits). The digit size was fixed but the number of rarebits per segment varied. In this prospective cross-sectional study, the author administered the RDT to 47 patients with optic nerve or pathway disorders and 30 normal controls. Visual acuity (VA) and visual field (VF), using high-pass resolution perimetry, were also assessed. The RDT results correlated modestly with VA and VF results. Using the receiver operating characteristic curve analysis, RDT was identified to have a larger area under curve than VA or VF, which meant RDT was the test with the best discrimination power. This test is available free on the Internet and it can potentially serve as a quick and cheap screening test.

Carmen Chan

INVESTIGATIONS WARRANTED FOR ISOLATED THIRD, FOURTH, AND SIXTH CRANIAL NERVE PALSIES

Tamhankar MA, Biousse V, Ying GS, Prasad S, Subramanian PS, Lee MS, Eggenberger E, Moss HE, Pineles S, Bennett J, Osborne B, Volpe NJ, Liu GT, Bruce BB, Newman NJ, Galetta SL, Balcer LJ. Isolated third, fourth, and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study. *Ophthalmology* 2013;120:2264–2269.

Acute onset isolated third, fourth, and sixth cranial nerve (CN) palsies in older individuals are often presumed to be of microvascular origin. To investigate or not to investigate, that is the question. In this prospective, multicentre, observational case series, the authors looked at 109 patients aged at least 50 years with isolated CN3 ($n=22$), CN4 ($n=25$), or CN6 ($n=62$), with or without pain, within 1 month of onset and determined the aetiology by magnetic resonance imaging (MRI) with and without contrast, and clinical examination by a neuro-ophthalmologist. Eighteen patients (16.5%) were diagnosed with a nonmicrovascular cause (e.g., giant cell arteritis, neoplasm, inflammation, etc.), 11 of whom also had vasculopathic risk factors. When the patients were divided into those with a significant past medical history (e.g., cancer, immunosuppression, etc.; Group 1, $n=29$) and those with vasculopathic risk factors alone (Group 2; $n=80$); 8 (10%) of Group 2 were revealed to have a nonmicrovascular cause for their ocular motor nerve palsies. For Group 2 patients, when patients with GCA and CN3 palsies were excluded ($n=64$), other causes were identified in 3 (4.7%) of the patients. Based on the results of this study, the authors recommended laboratory workup and MRI in patients with isolated ocular motor nerve palsies. However, for patients with isolated CN4 or CN6 with vasculopathic risk factors alone,

the yield is relatively lower and there may be an argument for reserving the investigations/MRI for persistent nerve palsies, if there are financial constraints.

Carmen Chan

SUPERIOR OBLIQUE PALSY—A RARE COMPLICATION OF SKULL BASE SURGERY

Grabe HM, McKean EL, Eggenberger ER, Trobe JD. Persistent diplopia and superior oblique muscle dysfunction following dissection of the orbital periosteum in cranial base surgery. *Br J Ophthalmol* 2013;97:1330–1332.

A bicoronal skin flap is often used for anterior skull base and craniofacial surgery. As part of this procedure, the trochlea is usually dissected off the medial orbital wall, together with the periorbital. The periorbital is not surgically reattached at the end of the procedure, but left to adhere naturally back to the orbital wall. In this case series, the authors described 6 cases of unilateral superior oblique palsy after skull base surgery, out of an estimated 160 similar open cranial base procedures, presented to a single centre, over an 8-year period. Follow-up information was available in 4 patients, in whom the misalignment did not completely resolve. The authors postulated that the superior oblique palsy did not result from a neurologic cause, but from malposition of the trochlea. Although this is a rare complication, the possibility of persistent diplopia should be discussed as part of the informed consent before this type of neurosurgery.

Carmen Chan

OPTIC NERVE HEAD HAEMOGLOBIN LEVEL MEASUREMENT— A NEW METHOD TO QUANTIFY OPTIC ATROPHY?

Bambo MP, Garcia-Martin E, Perez-Olivan S, Sigut J, Fumero F, Fuentes JL, Ara JR, Martin J, Larrosa JM, Gonzalez-De la Rosa M. Diagnostic ability of a new method for measuring haemoglobin levels in the optic nerve head in multiple sclerosis patients. *Br J Ophthalmol* 2013;97:1543–1548.

Optic disc pallor is an objective sign of optic atrophy but it is difficult to quantify. The disc colour on fundus photos is affected by factors such as media opacity and photograph exposure. “Laguna ONhE” is a computer software which allows the measurement of the amount of haemoglobin (Hb) in different sectors of the optic nerve head (ONH) from conventional fundus photos. It quantifies the colour change of the disc, whilst compensating for illumination and lens absorption, by using the central retinal vessel colour as the reference value. The disc colour/Hb level is expressed as a percentage of the colour/Hb of the central retinal vessel. In this prospective cross-sectional study, the optic disc photos of 38 eyes of 38 patients with multiple sclerosis (of which 12 had a history of optic neuritis) were examined with this Laguna ONhE software, and compared with 40 eyes of 40 normal patients (all white Europeans). It was found that multiple sclerosis (MS) patients had significantly lower ONH Hb percentage in most sectors of the optic disc compared with normals, particularly in the temporal sectors. There was also good reproducibility. Therefore, the ONH Hb measurements can potentially be used to quantify optic atrophy and it has the advantage of not requiring any specialist equipment such as the optical coherence tomography (OCT) system. It would be interesting to see how the measured ONH Hb level correlates with peripapillary retinal nerve fibre layer thickness and whether the software can work in patients of other ethnic origins.

Carmen Chan

WHAT MIGHT OVAL PUPILS MEAN?

Mittalm MK, Rabinstein AA, Wijedicks EFM. Pearls & Oysters: Oval pupil. Two observations. *Neurology* 2013;81:e124–e125.

Oval pupils can be caused by either ophthalmologic or intracranial conditions. The authors reported nonreactive oval-shaped pupils in two unconscious patients. One patient presented with massive intracerebral

haemorrhage and died not long afterwards. The other patient had an acute infarction in the ipsilateral paramedian midbrain.

Panitha Jindahra

RETINAL CHANGES IN ALZHEIMER'S DISEASE

Marziani E, Pomati S, Ramolfo P, Cigada M, Giani A, Mariani C, Staurengi G. Evaluation of retinal nerve fiber layer and ganglion cell layer thickness in Alzheimer's disease using spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2013;54:5953–5958.

The study aimed to evaluate retinal involvement in patients with Alzheimer's disease (AD). By using RTVue-100 and Spectralis optical coherence tomography, the thickness of the inner retinal nerve fibre and ganglion cell layers (RNFL + GCL), and the thickness of the macular area were measured, respectively. Measurements were performed in AD patients ($n = 21$) and age-matched healthy subjects ($n = 21$). The RNFL + GCL and macular RNFL thickness were significantly decreased in AD patients compared with the control group. The findings were consistent with pathological studies that showed macular degeneration in AD. It is an interesting study and further investigations are required.

Panitha Jindahra

ERG FINDINGS IN LHON

Ziccardi L, Sadun F, Negri AM, Barboni P, Savini G, Borrelli E, Morgia CL, Carelli V, Parisi V. Retinal function and neural conduction along the visual pathways in affected and unaffected carriers with Leber's hereditary optic neuropathy. *Invest Ophthalmol Vis Sci* 2013;54:6893–6901.

Pattern electroretinograms (PERGs) and visual evoked potential (VEP) were performed in 39 patients with Leber's hereditary optic neuropathy (LHON) mutation (22 LHON-unaffected eyes and 17 LHON-affected eyes) and 22 age-matched healthy subjects. Age ranged from 20 to 45 years. The study demonstrated small PERG P50–N95 amplitudes in the LHON-unaffected group as compared with the controls. The results suggested subclinical retinal ganglion cell (RGC) dysfunction. PERG and VEP were markedly impaired in the LHON-affected group. Further studies are required to see whether PERGs could be a potential biological marker for LHON and that there might be a chance to introduce early treatment before losing vision.

Panitha Jindahra

AN EVALUATION OF PURPORTED RISK FACTORS IN OPTIC NERVE HYPOPLASIA

Garcia-Filion P, Borchert M. Prenatal determinants of optic nerve hypoplasia: review of suggested correlates and future focus. *Surv Ophthalmol* 2013;58:610–619.

Numerous risk factors have been implicated in the pathogenesis of optic nerve hypoplasia, including prenatal exposure to recreational and pharmaceutical drugs, maternal disease, and pathologic gene mutations. In their systematic review of the topic, the authors assert that commonly held beliefs about the teratogenicity of alcohol, anticonvulsants, and other substances may be founded on anecdotal evidence. Although a number of epidemiologic studies and case series have been published on the subject, they maintain that only primiparity and young maternal age have been established as sound potential contributors to optic nerve hypoplasia. One noted objection to some prior work is the fact that retrospective epidemiologic studies suffer from recall bias: mothers of affected children have a propensity to better remember untoward exposures. They also argue that many genetic linkage studies are complicated by the "loosening" of the definition of "septo-optic dysplasia" to include patients with midline brain malformations or hypopituitarism but no visual pathway disease. It is reaffirmed that optic nerve hypoplasia is likely caused by both genetic and environmental factors interacting in a complicated manner during a very sensitive period of fetal development. They close by asserting that further studies into this intricate cascade

of events should start with the two risk factors that have been reliably identified: primiparity and young maternal age.

Evan Price

STRABISMUS IS IN THE AMYGDALA OF THE OBSERVER

Berberat J, Jaggi GP, Wang FM, Remonda L, Killer HE. Changes in the amygdala produced by viewing strabismic eyes. *Ophthalmology* 2013;120:2125–2129.

The consequences of strabismus are far-reaching and include elements in the realms of health, visual performance, self-esteem, and interpersonal communication. The psychosocial aspects in particular are widely noted to be significant, but the cognitive neuroscience behind them has not yet been fully explored. In this functional magnetic resonance imaging (fMRI) study, the authors attempt to show that strabismus creates a measurable response in the brain of the observer. Normal subjects were shown blocks of images consisting of strabismic eyes, orthotropic eyes, or a neutral image (a crosshair on a blank screen), and the difference in blood oxygenation level–dependent (BOLD) signal was compared between these different viewing conditions. Of the 31 subjects, 30 had significant limbic activation when viewing strabismic eyes as compared with control eyes, including activity in the left amygdala and the bilateral parahippocampal gyri, hippocampi, and fusiform gyri. In fact, the one subject who did not show significant limbic activation was an ophthalmologist who played a role in designing the study. Stemming from the fact that the amygdala is strongly activated in the processing of fear, disgust, and other negative emotions, the authors assert that strabismus elicits a negative response in the observer on an organic and subconscious level. Furthermore, they report that more than one fourth of the volunteers reported no emotional response to viewing images of strabismus, even though the above pattern of limbic activation was noted in nearly all subjects. The authors argue that surgery to correct strabismus has the potential to improve relationships on the grounds that it has an organic effect on both the patient and the observer.

Evan Price

AN UPDATE ON AQP4-IGG SEROSTATUS-RELATED CHARACTERISTICS IN NEUROMYELITIS OPTICA USING SECOND-GENERATION ASSAYS

Jiao Y, Fryer JP, Lennon VA, Jenkins SM, Quek AM, Smith CY, McKeon A, Costanzi C, Iorio R, Weinshenker BG, Wingerchuk DM, Shuster EA, Lucchinetti CF, Pittock SJ. Updated estimate of AQP4-IgG serostatus and disability outcome in neuromyelitis optica. *Neurology* 2013;81:1197–1204.

Serologic testing for neuromyelitis optica (NMO) has become an important component of the management of this debilitating disease. In this study from the Mayo Clinic, the authors present data regarding three second-generation recombinant aquaporin-4 immunoglobulin G (AQP4-IgG) tests in patients who were previously reported to be seronegative by tissue-based indirect immunofluorescence (IIF) assay. Of the 5349 Mayo Clinic patients tested from 2005 to 2011, 164 patients met criteria for NMO (163 of whom consented to involvement in the study), and 53 of these patients were seronegative by IIF. Upon testing with recombinant AQP4-IgG assays, sera from 30 of these 53 patients yielded positive results in at least one of the tests, bringing the total seronegative rate from 33% to 12%. The sexes were equally represented in this updated seronegative group, contrary to previous evidence that women outnumber men 2:1 in seronegative NMO. Seronegative patients were found to be 10 times more likely to present with simultaneous initial onset of optic neuritis (ON) and transverse myelitis and had attacks of ON more frequently. Importantly, they reported that serostatus did not play a significant role in relapse rate, interval to relapse from disease onset, attack severity, or time to long-term motor or visual disability. Over a median follow-up of 8.3 years, more than half of all NMO patients were legally blind in one eye and 15% were bilaterally blind. More than one-third required a cane to walk. These data are more favourable than those previously reported, and the authors suppose that this is due to a higher identification rate of NMO than in the days prior to AQP4-IgG testing, resulting in a larger proportion of patients on immunosuppressive therapy.

Evan Price

APPLES AND PEARS AND PSEUDOTUMOR

Schwartz R, Kliper E, Stern N, Dotan G, Berliner S, Kesler A. The obesity pattern of idiopathic intracranial hypertension in men. *Graefes Arch Clin Exp Ophthalmol* 2013;251:2643–2646.

This article discusses the relationship of fat distribution in the body in persons with idiopathic intracranial hypertension (IIH). Subjects included 22 men with IIH, 60 men without IIH, and 44 women with IIH. The authors compared ‘gynecoid’ obesity (pear-shaped bodies), in which subcutaneous fat deposition is in the lower body, with ‘central’ obesity (apple-shaped bodies), in which fat deposition is abdominally predominant. Results showed that in females with IIH, 80% had the gynecoid fat pattern. In males with IIH, 55% had the gynecoid fat pattern. However, in men without IIH, only 35% had the gynecoid fat pattern. The conclusion of their report is that although a greater share of women than men with IIH have a gynecoid pattern, men with IIH are more likely to have a gynecoid pattern than men without IIH. If central obesity is ‘protective’ against IIH, this may explain why fewer men have IIH than women.

John H. Pula

DISK DRUSEN IN CHILDREN

Noval S, Visa J, Contreras I. Visual field defects due to optic disk drusen in children. *Graefes Arch Clin Exp Ophthalmol* 2013;251:2445–2450.

This study included 15 children (age 7 to 17), and 28 eyes with optic disk drusen. Twelve eyes had buried drusen, 8 had superficial drusen, and 8 were partially superficial. OCT showed that retinal nerve fibre layer (RNFL) thickness was decreased in the superficial drusen eyes, but was higher in the buried and partial drusen eyes. Only two eyes have normal visual field testing. Field defects included enlarged blind spots (5), nasal defects (15), and generalized constriction (6). The visual field defects were more pronounced in eyes with superficial drusen. Temporal RNFL fibres were less affected than the other three quadrants, which may explain the relative preservation of central acuity with optic disk drusen.

John H. Pula

A CASE OF ISOLATED SUSAC OCCLUSIVE RETINAL VASCULITIS

Seamone ME, Fielden M. A case of isolated Susac occlusive retinal vasculitis. *J Neuroophthalmol* 2013;33:260–262.

Susac syndrome is characterized by encephalopathy, sensorineural hearing loss, and branch retinal artery occlusion. The authors present a 51-year-old Caucasian woman with Susac syndrome in the setting of tinnitus and migraine with aura.

Michael Vaphiades

PARTIAL THIRD NERVE PALSY AND OCULAR NEUROMYOTONIA FROM DISPLACEMENT OF POSTERIOR COMMUNICATING ARTERY DETECTED BY HIGH-RESOLUTION MRI

Cruz FM, Blitz AM, Subramanian PS. Partial third nerve palsy and ocular neuromyotonia from displacement of posterior communicating artery detected by high-resolution MRI. *J Neuroophthalmol* 2013;33:263–265.

The authors report a 75-year-old woman with intermittent left-gaze-evoked binocular diplopia. She had an incomplete right third nerve palsy but became symptomatically diplopic and esotropic upon sustained left gaze. High-resolution magnetic resonance imaging (MRI) showed displacement of the right posterior communicating artery and contact with the right third nerve. Gaze-evoked diplopia resolved with carbamazepine, but a partial third nerve paresis remained. Ocular neuromyotonia is an unusual condition in which sustained, undesired contraction of one or more extraocular muscles occurs after normal muscle activation. Although most commonly

reported after parasellar cranial irradiation for tumour, chronic nonaneurysmal vascular compression of the third nerve can produce partial ocular motor nerve paresis and ocular neuromyotonia.

Michael Vaphiades

RECOGNITION AND MANAGEMENT OF STROKE IN YOUNG ADULTS AND ADOLESCENTS

Singhal AB, Biller J, Elkind MS, Fullerton HJ, Jauch EC, Kittner SJ, Levine DA, Levine SR. Recognition and management of stroke in young adults and adolescents. *Neurology* 2013;81:1089–1097.

The authors review ischaemic strokes occurring in young adults and adolescents and comment on the American Academy of Neurology's consensus document concerning recognition, evaluation, and management.

Michael Vaphiades

BILATERAL VISION LOSS RESPONSIVE TO CORTICOSTEROIDS

Lee MD, Song BJ, Odel JG, Sadun AA. Bilateral vision loss responsive to corticosteroids. *Surv Ophthalmol* 2013;58:634–639.

The authors report a 48-year-old woman with steroid responsive painless nonsimultaneous bilateral vision loss. The diagnosis was confounded by a by a negative workup for multiple sclerosis (MS) and a positive test for Leber hereditary optic neuropathy (LHON). Several months later she developed a myelopathy and the disease declared itself as MS. The differential diagnosis of LHON and other entities are discussed.

Michael Vaphiades

A POX UPON YOUR HOUSE

Hashemi N, Zhang J, Volpi J, Lee AG, Gordon LK. A pox upon your house. *Surv Ophthalmol* 2013;58:640–643.

Herpes zoster ophthalmicus is a common viral infectious disorder affecting the ophthalmic division of the trigeminal nerve. A small subset of these patients present with the ophthalmic symptoms, but without an accompanied rash (Herpes zoster sine herpete). The authors report a patient presenting with trigeminal pain, uveitis with progression to encephalitis, and bilateral cerebral infarctions despite treatment with acyclovir and corticosteroids. The diagnosis of herpes zoster ophthalmicus sine herpete was confirmed by polymerase chain reaction testing on the cerebrospinal fluid.

Michael Vaphiades

PIPELINE EMBOLISATION DEVICE: A NEW SOURCE FOR EMBOLIC RETINAL VASCULAR OCCLUSION

Sise AB, Osher JM, Kolsky MP, Stemer A, Bank WO, Garfinkel RA. Pipeline embolization device: a new source for embolic retinal vascular occlusion. *J Neuroophthalmol* 2013;33:373–376.

The authors present a 57-year-old woman who underwent treatment of a left internal carotid artery aneurysm with a pipeline embolisation device who subsequently experienced multiple branch retinal artery occlusions in her left eye. Although rare, ophthalmic complications may follow this new technique in the treatment of intracranial aneurysms.

Michael Vaphiades

**BILATERAL NONARTERITIC ANTERIOR ISCHAEMIC OPTIC NEUROPATHY:
COMPARISON OF VISUAL OUTCOME IN THE TWO EYES**

Hayreh SS, Zimmerman MB. Bilateral nonarteritic anterior ischemic optic neuropathy: comparison of visual outcome in the two eyes. *J Neuroophthalmol* 2013;33:335–340.

The authors investigated 174 consecutive patients with bilateral nonarteritic anterior ischaemic optic neuropathy (NA-AION) to determine if the visual outcome is similar in the two eyes. Their results showed large differences between the visual acuity and visual field findings of paired eyes at initial and final visit, whether or not treated with steroids. They concluded that it is not possible to predict the visual acuity and visual field grade in the second eye based solely on the first eye.

Michael Vaphiades

DOWN BUT NOT OUT

Kim JD, Crockett C, Diaz O, Lee AG, Miller NR. Down but not out. *Surv Ophthalmol* 2013;58:644–651.

The authors report a 20-year-old Hispanic man with Down syndrome presenting with headache, visual loss, and papilloedema. Magnetic resonance venography showed thrombosis of left transverse and sigmoid sinuses. Catheter angiography angiogram showed a dural arteriovenous fistula in the wall of left transverse and sigmoid sinuses. The patient underwent Onyx endovascular embolisation of the fistula that resulted in resolution of his symptoms.

Michael Vaphiades