Potential diagnostic dilemmas using the multifocal electroretinogram in intermittent exotropia

Multifocal electroretinography (mfERG) is a valuable technique in assessing macular function in retinal disease objectively as it provides spatial information. Altered responses give an estimate of the extent of central retinal dysfunction. Fixation is known to be an important technical factor in mfERG recording. We present findings in a patient with asymptomatic intermittent exotropia that reinforce the importance of adequate consideration of potential fixation errors.

Case report

The patient was a 52 year old man with maternally inherited diabetes and deafness (MIDD) consequent upon a mitochondrial DNA nucleotide A3243G point mutation, and examined as part of a series of patients with MIDD. Visual acuity was 20/20 (ETDRS chart) bilaterally. Fundi showed symmetrical macular function was assessed initially by mfERG recorded binocularly with a stimulus size of 61 hexagons using the RETIscan System (Roland Consult, Wiesbaden, Germany). The patient fixated on the centre of a large diagonal cross, centred over the central hexagon, at a viewing distance of 33 cm. Pupils were dilated. Refractive errors were corrected with −0.75 + 6.25 × 180 dioptres base-in at 33 cm. A small vertical deviation. At times of positive binocular vision the fixation was located almost centrally. The fixation was slightly shifted because of the microtropia (fig 1B) which was not detected by direct observation. Examiners should always be aware that not only retinal disease can affect the mfERG. Asymptomatic strabismus is a reason for fixation instability and represents a potential dilemma in the interpretation of binocular mfERGs. Even with direct observation a small intermittent strabismus may be not be detected. This could result in a broadened central peak rather than the double peak seen in our patient and thus be mistaken for macular dysfunction. This would be potentially disastrous in a patient with optic nerve disease where the mfERG should be normal.

Comment

Patients with intermittent exotropia can be completely controlled having binocular vision or may have a manifest exotropia. Under binocular mfERG stimulation, the left eye presumably fixated in exotropia at times of fusional decompensation, and the stimulus pattern shifted by the extent of the squint deviation. At times of positive binocular vision the fixation was located almost centrally. The fixation was slightly shifted because of the microtropia (fig 1B) which was not detected by direct observation. Examiners should always be aware that not only retinal disease can affect the mfERG. Asymptomatic strabismus is a reason for fixation instability and represents a potential dilemma in the interpretation of binocular mfERGs. Even with direct observation a small intermittent strabismus may be not be detected. This could result in a broadened central peak rather than the double peak seen in our patient and thus be mistaken for macular dysfunction. This would be potentially disastrous in a patient with optic nerve disease where the mfERG should be normal.

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Figure 1 (A) Three dimensional plot (left) and trace arrays (right) of the right eye recorded binocularly. See text for details. (B) Left eye under binocular recording. On the three dimensional plot (left) the left peak is consistent with fixation in exotropia. At times of positive binocular vision the fixation is almost centrally located (right peak). Trace array changes are seen in most hexagons (right).
Partial resolution of diabetic macular oedema after systemic treatment with furosemide

Furosemide is a potent diuretic which is an anthranilic acid derivative. Chemically, it is 4-chloro-N-furfuryl-5-sulfamoylanthranilic acid. Furosemide is indicated for the treatment of oedema associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome. Here I report a case of a diabetic patient, with nephrotic syndrome, who experienced marked improvement in diabetic macular oedema after systemic treatment with furosemide.

Case report

A 41 year old woman with type II insulin dependent diabetes mellitus was referred for decrease in vision in both eyes over the past 2 months. Besides the diabetes, her past medical history was positive for irregular menstrual cycle and gastroparesis. The patient had also noticed a gain in weight of about 30 lb (13.5 kg) over the same period of time, from 154 lb (69.3 kg) to 196 lb (89.3 kg). Three weeks later her vision had improved to 20/80 in both eyes. On fundus examination there was marked improvement in the macular oedema in both eyes. OCT examination confirmed the partial resolution of the macular oedema. The central retinal thickness measured by OCT was 250 μm in the right eye and 218 μm in the left eye.

Comment

Diabetic macular oedema is characterised by hyperpermeability of retinal blood vessels and subsequent formation of hard exudates and macular oedema, the degree of which can be estimated by measurement of retinal thickness. The severity and progression of diabetic macular oedema has been associated with the presence of nephrotic syndrome and to the degree of proteinuria. In a recent study, the central retinal thickness measured by OCT was 763 μm in the right eye and 722 μm in the left eye (fig 2A–B). The patient was offered grid laser treatment for the macular oedema, but she did not feel well and she refused the treatment. A follow up appointment was arranged for 3 weeks’ time.

The following day the patient presented to the emergency room complaining of nausea and weakness. She was admitted to the hospital with a diagnosis of nephrotic syndrome and fluid overload. Her albuminuria level was 330 mg/l (normal value <12 mg/l). She was treated with systemic furosemide 40 mg twice a day for 2 weeks. A few days after starting the treatment with furosemide she began to lose weight. She also noticed an improvement in her vision. In 3 weeks the patient lost 30 lb (13.5 kg) and she had returned to her usual weight of 154 lb (69.3 kg). Three weeks later her vision had improved to 20/80 in both eyes. On fundus examination there was marked improvement in the macular oedema in both eyes. OCT examination confirmed the partial resolution of the macular oedema. The central retinal thickness measured by OCT was 250 μm in the right eye and 218 μm in the left eye (fig 2C, D).

References


We thank Roland Consult for mFERG facilities.
Nephrotic syndrome is characterised by massive proteinuria, which leads to hypoalbuminaemia, hyperlipidaemia with elevated cholesterol, triglycerides and other lipids, and oedema. The oedema results not only from the hypo-osmolar state caused by the loss of plasma proteins, but also from abnormal salt and water retention. Furosemide is used in the treatment of fluid overload experienced by patients with nephrotic syndrome because it is a potent and rapid acting diuretic. It has been demonstrated that furosemide inhibits primarily the absorption of sodium and chloride not only in the proximal and distal tubules but also in the loop of Henle. I reported what is, to my knowledge, the first case of marked improvement of diabetic macular oedema after systemic treatment with furosemide documented by OCT examination. I think that the fluid overload secondary to the nephrotic syndrome was the main cause of the worsening of the macular oedema in this patient, and that the intense treatment with furosemide was responsible for reducing the amount of fluid overload and resolving the macular oedema. The exact mechanism of the action of furosemide in resolving the macular oedema is unknown. Tsuboi et al demonstrated that furosemide inhibits fluid absorption across retinal pigment epithelium (RPE) in an experimental model of retinal detachment monkeys. According to their study furosemide could worsen the presence of a neurosensory macular detachment especially in a patient where the subneurosensory retina fluid collection is secondary to a defect in RPE pump. However, the FA study of this patient at presentation demonstrated multiple retinal microaneurysms at the posterior pole of both eyes and diffuse intraretinal microvascular leakage of dye in the late phase of the study. The FA study was consistent with the appearance of diffuse diabetic macular oedema. In such cases the intraretinal and subneurosensory retina leakage of dye is secondary to a microvascular retinal defect and not to a failure in the RPE pump. I think that restoration of more normal oncotic pressure within the retinal vasculature was the underlying reason for the response to the drug of the diabetic macular oedema.

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Vision loss as a complication of gamma knife radiosurgery for trigeminal neuralgia

Gamma knife radiosurgery has been found useful for treatment of trigeminal neuralgia (TN).Although it is generally safe and well tolerated by most patients, adverse effects have been reported. Potential ocular complications include “dry eye” and “corneal numbness.”6,7 We describe a case of vision loss that occurred 9 months after gamma knife radiosurgery for TN.

Case report

A 68 year old man presented in September 2003 with 3 weeks of fluctuating blurred vision in the right eye. The blurring began 3 weeks earlier and had been preceded by complete numbness of the right side of his face for 1 week.

The patient’s medical history was remarkable for right sided TN that began in 1998, predominantly involving the V2 dermatome. It had been managed medically at first but eventually became incapacitating and led to hospital admission.

In December 2002, he had undergone gamma knife radiosurgery (Leksell Gamma Knife; Elekta Inc, Norcross, GA, USA). The dose matrix grid was 0.6 mm and the right trigeminal root entry zone was targeted tangential to the brainstem. The prescription dose was 40 Gy to the 50% isodose line. A single run with a single shot (treatment time, 29.25 minutes) used a 4 mm collimator. Within days, the patient had clinically significant improvement in symptoms, was pain free, and required no pain medication.

The patient also had a history of chronic renal failure requiring dialysis three times weekly, hypertension, a myeloproliferative disorder, prostate cancer, and hyperlipidaemia. In 1998, he had resection of a left frontal lobe meningioma. His ocular history included bilateral cataract surgery but no history of herpes zoster or herpes simplex.

On initial examination, his vision measured 20/25 right eye and 20/25 left eye. Slit lamp examination of the right cornea revealed a fine punctate epitheliopathy (fig 1A). Corneal sensation, tested with a Cochet-Bonnet aesthesiometer (Luneau Ophthalmologie, Chartres Cedex, France), was absent even at a 5 mm filament length, both subjectively and by blink reflex. Sensation in the left cornea was present at a 60 mm filament length.

The patient’s vision gradually declined despite treatment with preservative free artificial tears and placement of a punctal plug in the right lower lid. Ten weeks after presentation, his vision measured 20/200 right eye and 20/25 left eye. Slit lamp examination revealed severe epithelial keratopathy in the right eye (fig 1B). Fourteen months after radiosurgery, TM weighted magnetic resonance imaging showed increased signal intensity in the anterior aspect of the right fifth nerve (fig 2).

A punctal plug was placed in the right upper lid. The patient began using topical serum tears four times daily. Partial tarsorrhaphy was discussed with the patient but
Our patient had a vision loss to 20/200 associated with the onset of right sided facial numbness 10 months after low dose (40 GY) gamma knife radiosurgery for TN. Although a high dose radiosurgery (90 GY) is a known risk factor for complications with gamma knife radiosurgery, the low dose our patient received has not been associated with such complications. Patients undergoing gamma knife radiosurgery for TN should be warned of this potential complication and should be evaluated preoperatively and postoperatively by an ophthalmologist.

Comment

Gamma knife radiosurgery is an effective treatment for TN with few complications. Pollock et al noted an increased incidence of “trigeminal dysesthesia” and “corneal numbness” after high doses (90 GY) of gamma knife radiation. In an animal model, a 100 Gy dose caused nerve necrosis, Matsuda et al identified a “dry eye complication” of epithelial keratopathy after gamma knife radiosurgery for TN. Despite these documented ocular side effects, no cases of vision loss have been reported.

Neurotrophic keratopathy has been recognised in patients with herpes simplex, herpes zoster, and after laser in situ keratomileusis (LASIK) surgery. Mild neurotrophic keratopathy may be manifested as a punctate epithelial keratopathy. In severe cases, corneal decompensation can lead to severe vision loss.

Figure 1
(A) Neurotrophic punctate epithelial keratopathy in the right eye at presentation.
(B) Advanced neurotrophic keratopathy 10 weeks after initial presentation.

Figure 2
T2 weighted magnetic resonance imaging shows increased signal intensity in anterior aspect of right fifth nerve.

departmental concerns were raised by experience with a 76 year old normotensive patient who was on COM. He developed progressive zonal dialysis from unexpected vitreous pressure during standard phacoemulsification. An intracapsular extraction and anterior vitrectomy were required. An iridectomy led to extensive intraoperative hypachema and vitreous haemorrhage. Postoperative ultrasound confirmed no evidence of choroidal haemorrhage, and the vitreous blood cleared within 3 months to produce 6/6 Snellen acuity with aphakic contact lens correction.

There is a lack of adequate data on the risk of surgery associated ocular bleeding with COM. Clopidogrel taken alone causes less gastrointestinal haemorrhage than aspirin, but has an otherwise similar risk profile to aspirin.

Post-marketing surveillance of clopidogrel has recorded “conjunctival, ocular, and retinal haemorrhage.” Further information regarding these events, and whether they occurred during ocular surgery, was not available at the time of writing (November 2004). A detailed Medline literature search has produced no relevant ophthalmic case experience.

The CURE study found higher “major and minor” bleeding rates in patients taking COM compared with aspirin alone, but showed no increase in life threatening or intracranial haemorrhage, and does not record ocular haemorrhage. Of note is the significant increase in major bleeding events recorded in COM patients undergoing coronary artery bypass graft surgery where the clopidogrel was stopped less than 5 days before the procedure.

A February 2004 telephonic survey of nursing staff running cataract pre-assessment clinics at 13 ophthalmic units across the United Kingdom indicated that local approaches to such agents. Individual consultants at three units stopped clopidogrel preoperatively. Twelve units continued clopidogrel; none had specific policy for patients on aspirin and clopidogrel. The related and relevant issue of anaesthetists’ approach to regional ocular anaesthesia in patients on such treatment was not addressed.

Translating the CURE study results into a “number needed to treat” of approximately 47 patients with acute coronary syndrome would require treatment for 9 months with aspirin and clopidogrel to prevent one cardiovascular death, non-fatal myocardial infarction, or stroke. Stopping clopidogrel for a short period is therefore unlikely to make a material difference to the vascular event risk for an individual.

In summary, there is an increased risk of systemic bleeding associated with COM compared to aspirin alone. The degree of perioperative bleeding risk with elective eye surgery is still undefined. Our departmental policy has been changed to stopping clopidogrel for 1 week in patients on combination treatment given for cataract surgery, and to use a similar approach to that normally
employed for patients taking aspirin in those on clopidogrel alone. Other departments’ experience with this increasingly used antiplatelet agent would be valued.

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The role of corticosteroids in fungal keratitis: a different view

Fungal infections of the cornea continue to be an important cause of ocular morbidity.1 This report describes a situation which occurs in clinical practice in patients with misdiagnosed fungal ulcers who are treated with a combination of topical steroids and antibiotics drops. A common strategy when these cases are finally diagnosed with fungal keratitis is to switch to antifungal agents and discontinue the corticosteroids. We have recently seen two patients with fungal keratitis who demonstrated severe inflammation and corneal necrosis after the abrupt discontinuation of corticosteroids.

Case 1

A 32 year old woman with a corneal transplant in her right eye was referred for evaluation of an unresponsive corneal ulcer. The patient had been treated for 2 weeks with cefazolin 50 mg/ml and tobramycin 0.3% on an hourly basis, prednisolone 1% five times per day, and ketoco-
nazole 400 mg by mouth. On initial examination there was a diffuse central stromal infiltrate associated with the pre-
seon of an endothelial plaque and hypopyon.

We performed confocal microscopy which showed hyphae characteristic of a fungal infection. After cultures were taken we modified the therapeutic regimen to fluconazo-


Authors’ qualifications and the BJO

It is not often that journal policy is dictated by input from the readership. A notable exception to this probably occurred in the

Case 2

A 13 year old girl who was a soft contact lens wearer was referred for evaluation of a corneal ulcer. The patient had been treated

ANZ Journal of Surgery in 2002, following a letter to the editor in 2001 addressing authors’ qualifications.1 In we pointed out that journal aspira-
tions to international recognition and increased circulation may be enhanced by having the authors’ qualifications consist-
tently published. We indicated that the qualifications of one’s own institution’s clinical staff, or colleagues—for instance, a clinician’s higher qualifications (for example, PhD) may be determined. We pointed out that the reader can determine whether the author is in effect a qualified ophthalmologist, a resident, or still a medical student. In some parts of the world, the rivalry between optometrists and ophthalmologists may be highlighted by one group publishing in the other’s journal. Thus, qualifications may be used to discriminate between the two groups. Where the qualifi-
cation discriminates between physicians and surgeons, this too can be recognised. In these days of enhanced medicolegal confrontation, a medical practitioner’s viewpoint can be better assessed if the author qualifications are designated, the reader may be quite sure that the article was not written by the medical records librarian, let alone the hospital trolley boy in a moment of inspiration.

We have observed that in recent issues of the BJO, there appears to be an inconsistent approach to appending qualifications. Only the corresponding author is liable to be given a qualification; the first author usually goes without. For example in volume 88 number 5 (May 2004), in the perspective, only the corresponding author, Azuara-Blanco writing on cannabinoids and glaucoma received a qualification.

In the extended reports, only Miyamoto on oil droplets in rabbits, Shaarawy on day one intraocular pressure, Orgul on blood flow in glaucoma, and Probst on fibronectin in diabetic rats received recognitions; recognitions that the authors of all the other extended reports missed out. In other words, in this issue of the journal, only one third of the corresponding authors, let alone the co-

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References
We read with interest the report of Hsuan et al. The authors state that their patients were happy to have multiple operative sessions. For patients undergoing Mohs micrographic surgery, complete tumour removal is accomplishment in one session, with reconstruction performed on the same day as tumour extirpation. The inconvenience to patients associated with staged re-excision after 48 hours of histological examination and then a final stage reconstruction 48 hours after the last histological sample is taken should not be underestimated. Patients in general are pleased with their care based primarily with their interaction with the physicians. Unfortunately, we doubt that any patient would choose three surgical interventions over 5 days rather than one surgical intervention with 100% margin control in 1 day.

The authors state that Mohs surgery is “too expensive.” This statement is unsubstantiated. In a cost analysis by Cook and Zitelli, Mohs surgery was found to be similar in cost to excisional surgery and less expensive than frozen section analysis. With three potential operative encounters, the cost of staged excision of basal cell carcinoma in the United States would exceed that for Mohs micrographic surgery with reconstruction on the same day. It is also important to note that the pathological charges are included in the Mohs surgery fee, as the Mohs surgeon is expert in the complete removal of complex skin cancers, particularly on the central facial area. Mohs surgeons work closely with our colleagues in oculoplastic surgery in the United States to coordinate expert reconstruction of the resultant defects. In places where Mohs surgery is less available, close communication between the surgeon and pathologist, and tangential vertical margin processing may offer a reasonable therapeutic option, although one that is more inconvenient, costly, and laborious for patients and physicians alike.

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We believe that the evidence presented in our article, that cefazidime currently represents the best agent for the treatment of Gram negative microbes in endophthalmitis.

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LASIK in children?

O’Keefe and Nolan report on LASIK surgery in five children with unilateral high myopia who were presumed to have amblyopia. One subject had bilateral high myopia.

References

LASIK in children?

O’Keefe and Nolan report on LASIK surgery in five children with unilateral high myopia who were presumed to have amblyopia. One subject had bilateral high myopia.
Optic nerve hypoplasia is associated with high myopia. In addition, anisometropic myopia is a common sequela of retinopathy of prematurity. Thinning of the sclera with posterior staphyloplasia formation has long been known to be associated with high myopia. Best corrected visual acuity in these patients is often limited by associated retinal and choroidal pathology. None of the treated eyes obtained acuity better than 6/15. This limited outcome following refractive surgery may be because optical enlargement of the retinal image rather than enhanced neurosensory function. In the three children who were less than 3 years old improved literacy, familiarity with the test procedure, and the Hawthorn effect were certainly important factors in their assumed improvement. The absolute lack of progress in one child was a probable manifestation of pre-existing retinal pathology rather than non-compliance with patching.2,3 The authors advocate increased use of LASIK to thin the corneas of highly myopic children who already have profound reductions in scleral thickness. “From a clinical viewpoint, optic nerve hypoplasia should be carefully looked for in all patients with unilateral bilateral high myopia and visual loss.” It may well be more appropriate to improve the quality of retinal and optic nerve evaluations before performing irreversible surgical procedures with unknown long term consequences for these abnormal eyes.

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In the paper titled The severe acute respiratory syndrome coronavirus in tears (Br J Ophthalmol 2004;88:861–863) H-N Leong was not listed as an author. The authors should have been listed as, S-C Loon, S C B Tosh, L L E Oon, S-Y Se-Thoe, A-E Ling, Y-S Leo and H-N Leong. The journal apologies for this error.

CoRReCTIoNS

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The Royal National Institute of the Blind are permanently in great need of new, used, foreign, British and all other kinds of postage stamps. The stamps are sold to raise money for children in need of specially adapted toys and everyday gadgets, help for parents and the any other needs of blind and partially sighted children throughout the UK. Please send stamps (British and foreign stamps should be sent in separate envelopes) to the following address: RNIB, PO Box 6198, Leighton Buzzard, LU7 9XT.

Sunshine Fund for Blind Children

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Prestigious Helen Keller Foundation prize awarded to one of London’s most eminent ophthalmologists

Professor Alan Bird, Institute of Ophthalmology, University College London and Consultant Ophthalmologist at Moorfields Eye Hospital NHS Trust, has been awarded one of ophthalmology’s most prestigious prizes, the Helen Keller Prize for Vision Research. The prize was created in 1994 by the Helen Keller Foundation for Research and Education, based in the USA, and honours the scientists and researchers working in the field of blindness and visual loss. Professor Bird is one of the world’s leading experts on age related macular degeneration (AMD), inherited macular degeneration and Retinitis Pigmentosa (RP), and has led research into the identification of the genes which cause retinal degeneration. As well as his scientific research, Professor Bird also continues to treat patients at regular clinics at Moorfields Eye Hospital. Further information on Moorfields is available at: www.moorfields.nhs.uk. Further information about the Helen Keller Foundation is available at www.helenkellerfoundation.org. Further information on the Institute of Ophthalmology is available at www.ucl.ac.uk/ioo.

Sophie sees sight saving projects in Tanzania with VISION 2020

HRH The Countess of Wessex has recently returned from a trip to Tanzania in her role as Patron of VISION 2020: The Right to Sight. Throughout the trip The Countess met with representatives of and visited projects supported by VISION 2020 Partners, including Sight Savers International (SSI), Christian Blind Mission (CBM), International Eye Foundation, International Trachoma Initiative (ITI), Helen Keller International (HKI), International Centre for Eye Education (ICEE), the SEVA Foundation and the Killimanjaro Centre for Community Ophthalmology (KCCCO). VISION 2020: The Right to Sight is a global initiative of the International Agency for the Prevention of Blindness (IAPB) and the World Health Organization (WHO), with a coalition of international Non-Governmental organisations. VISION 2020 aims to eliminate unnecessary blindness in order to give all children the same opportunities, particularly the millions of needlessly blind, The Right to Sight. For further information, please visit www.v2020.org.