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.1-4 Fixation is known to be an important technical factor in mfERG recording.5 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 bilateral irregular patches of retinal pigment epithelium atrophy at the posterior poles. The foveas were normal.

Macular function was assessed initially by mfERG recorded binocularly with a stimulus size of 61 hexagons using the RETI-scan 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 −6.25 dioptres (D) right eye and −6.25 spherical dioptres combined with −0.75 cylindrical dioptres at 5° left eye. Additional +3D were given for a viewing distance of 33 cm. Each recording session consisted of eight trials over about 20 minutes.

Upon binocular recording, changes reflecting the retinal dystrophy were visible in the right eye trace array outside the central hexagon. The normal foveal response was consistent both with normal foveal function and central fixation throughout testing (fig 1A). Amplitude reduction was observed in many left eye traces with an additional “off centre” peak also visible in three dimensional plot (fig 1B). These findings are not suggestive of MIDD. The mfERG was repeated monocularly. The left eye findings now showed a normal central response and alterations in parafoveal function consistent with MIDD (fig 1A, C, D).

Subsequent orthoptic examination revealed a near type intermittent exotropia with poor motor fusion and additional microtropia. The latent deviation of the left eye was 2 prism dioptries base-in at 6 metres and 18 prism dioptres base-in at 33 cm. A small vertical height component was demonstrated on the Hess chart. Stereopsis was subnormal.

Comment

Patients with intermittent exotropia can be completely controlled having binocular vision or may have a manifest exotropia.6 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.1-4

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 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).

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Furosemide is a potent diuretic which is an approved treatment with furosemide for the systemic treatment of diabetic macular oedema after systemic treatment with furosemide.

Partial resolution of diabetic macular oedema after systemic treatment with furosemide

Furosemide is indicated for the treatment of oedema associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome.

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 (88.2 kg). She was treated with insulin for 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, 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 (88.2 kg). She was treated with insulin for 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.

**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.

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.

Supported by the European Commission No QLK6-CT2000-51262 (Marie Curie Individual Fellowship) and by the Faun-Foundation to CB.

We thank Roland Consult for mfERG facilities.

**References**


**Figure 2**

(A) Monocular mfERG recording of the right eye. (B) Monocular mfERG recording of the left eye. Changes reflecting MIDD are visible outside the central hexagon.
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). However, it is generally safe and well tolerated by most patients, adverse effects have been reported. Potential ocular complications include "dry eye" and "corneal numbness." 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, and hypercholesterolemia. He had type 1 diabetes, prostate cancer, and hyperlipidemia.

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 20/20 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 Ophtalmologie, 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 keratoconjunctivitis in the right eye (fig 1B). Fourteen months after radiosurgery, 12 weighted magnetic resonance imaging showed increased signal intensity in the anterior aspect of the right fifth nerve (fig 2).

A punchal 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 not undertaken.

References

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 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.

Combined aspirin and clopidogrel in cataract surgical patients: a new risk factor for ocular haemorrhage? Clopidogrel (PlaviX, Bristol-Myers Squibb/Sanofi) is a thienopyridine with antiplatelet effects caused by its inhibition of ADP mediated platelet aggregation pathways. Both aspirin and clopidogrel have established benefits in the secondary prevention of fatal and non-fatal coronary and cerebrovascular events. The CURE study has concluded that combining low dose aspirin and clopidogrel in patients with acute coronary syndromes results in additional improvements in outcome over aspirin alone. We can therefore expect increasing numbers of ophthalmic patients who have been started on this combined treatment (“COM”). Departmental concerns were raised by experience with a 76 year old normotensive patient who was on COM. He developed progressive zonular dialysis from unexpected vitreous pressure during standard phacoemulsification. An intracapsular extraction and anterior vitrectomy were required. An iridectomy led to extensive intraoperative hypphaema 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 15 ophthalmic units across the United Kingdom indicated a lack of guidance on perioperative bleeding risk with elective eye surgery. 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 15 ophthalmic units across the United Kingdom indicated a lack of guidance on perioperative bleeding risk with elective eye surgery. 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.

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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 in her transplant. The patient had been treated with a combination of moxifloxacin 0.5% drops hourly and prednisolone 1% drops four times per day. On initial examination there was a central stromal infiltrate with an overlying epithelial defect. The infiltrate had feathery edges reminiscent of fungal infection. The cultures had not been taken up to this point. After cultures were taken the therapeutic regimen was switched to cefazolin 50 mg/ml and gentamicin 15 mg/ml while we discontinued the corticosteroid drops. The clinical picture remained relatively unchanged during the next 48 hours. The preliminary culture results revealed fungal yeasts. We then started amphotericin 0.15% drops and fluconazole by mouth but the infection worsened over the next 2 days leading to descemetocele formation and perforation; the patient underwent an emergency keratoplasty.

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 for 2 weeks with cefazolin 50 mg/ml and tobramycin 0.3% on an hourly basis, prednisolone 1% five times per day, and ketocano- nazole 400 mg by mouth. On initial examination there was a diffuse central stromal infiltrate with the presence 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- zole by mouth, natamycin 5% drops, cefazolin 50 mg/ml while we discontinued the steroid drops. The patient showed signs of worsening during the next 2 days; the cornea perforated and an emergency keratoplasty was performed.

Comment
The analysis of the previous cases suggests that in patients with fungal keratitis who previously received topical corticosteroids, the abrupt cessation of these agents is likely to lead to an acute inflammatory reaction and even perforation.

The proper use of corticosteroids in the treatment of fungal corneal infections continues to be debated among experts.2 The controversy arises because there are two goals in the treatment of corneal infection that are inherently incompatible: (a) to rid the affected tissue of the replicating micro-organisms causing the infection, and (b) to limit the degree of structural damage caused by the infectious process.3

We recommend a gradual tapering of the corticosteroids in these cases which allows for the antifungal agents to act, and the host immune mechanisms to take control of the inflammatory response. However, clinical application in patients should be determined individually in all cases.

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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 ANZ Journal of Surgery in 2002, following a letter to the editor in 2001 addressing authors’ qualifications.4 In that instance we pointed out that journal aspirations to international recognition and increased circulation may be enhanced by having the authors’ qualifications consistently published. We indicated that the qualifications of one’s immediate associates, including departmental heads where one may have trained overseas, can be recognised. The educational progress of one’s 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 ophthalmologists 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 qualification discriminates between physicians and surgeons, this too can be recognised. In these days of enhanced medicolegal confrontation, a medical practitioner’s viewpoint can be differentiated from that of a lawyer.

Finally, we pointed out that if a 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, Azaurea-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 diabetes received qualifications, suggesting 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-author of extended reports, are given qualifications. No one in the letters section was designated with a qualification. None of the three editorial writers received a qualification.

We are left wondering as to whether Professor König, writing on the cost effectiveness of treatment for amblyopia, was a paediatric ophthalmologist branching out into community medicine, a medical politician, a health economist, a statistician, or a psychotherapist having a devil of a time. Whatever he is, he reached a reassuring conclusion in his article, that amblyopia therapy is “likely to be very cost effective.”5 We also do not know whether Schwab, writing about the “Halcyon days,” with the university affilia- tion of UC Davis, was an artist, the university photographer, an ornithologist, an anthropologist, or a Greenpeace officer. The article on postoperative leak in trabeculectomy, Henderson can be recognised as a surgeon by the British appellation “Mr.” We thus presume he has an FRCS or an FRCophth, but we don’t really know.

Our point is made. As we demonstrated in our original article,1 89.5% of the 19 journals regularly read by us use author qualifications.
We read with interest the report of Hsuan and colleagues 2004. We agree with their conclusion 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 cultures are included in the Mohs surgery fee, as the surgeons perform functions as both the surgeon and pathologist. Therefore, pathology charges generated for multiple staged re-excisions must be included in any calculation of cost associated with staged excision.

The authors characterised Mohs surgery as “laborious.” I would argue that one doctor performing a very efficient tissue sparing operation overall in a matter of 2–4 hours, a typical duration for Mohs surgery and reconstruction, with the pathology included within that time frame and fee, is both cost efficient and labour efficient. Mohs surgery has been especially designed for accuracy, tissue sparing, convenience, cost efficiency, and labour efficiency.

Mohs surgeons are expert in the complete removal of complex skin cancers, particularly on the central facial area. Mohs surgery, together with our colleagues in ocular plastic 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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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 staphyloma 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 chorioretinal 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 eye charts and reversal abilities, the authors advocate increased use of LASIK to thin the corneas of highly myopic children who already have profound reductions in sceral 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 letter titled Prospective case control study on genetic association of apolipoprotein e2 with intraocular pressure (Br J Ophthalmol 2004;88:581–582) the authors were listed incorrectly. The correct listing is as follows: A Jüinemann, S Bleich, U Reulbach, K Henkel, N Wakill, G Beck, B Rautenstrauss, C Mardim, G O H Naumann, A Reis, J Kornhuber. The journal apologises for this error.

4th International Congress on Autoimmunity
The 4th International Congress on Autoimmunity will take place 3–7 November 2004 in Budapest, Hungary. The deadline for the receipt of abstracts is 20 June 2004. Further details: Kennes International Global Congress Organisers and Association Management Services, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland (tel: +41 22 908 0488; fax: +41 22 732 2850; email: autoimm04@kennes.com; website: www.kennes.com/autoimm04).

XVI International Congress for Eye Research

Ophthalmic Anesthesia Society
The 18th Annual Meeting of the Ophthalmic Anesthesia Society will be held on 1 – 3 October 2004 in Chicago, USA. For further details: Ophthalmic Anesthesia Society (OAS), 793-A Foothill Blvd, PMB #119, San Luis Obispo, CA 93405 USA (tel: 001 805 534 0300; fax: 001 805 534 9030; email: info@eyeanesthesia.org; website: www.eyeanesthesia.org).

Glaucoma Society Silver Jubilee Meeting
2004
The Silver Jubilee Meeting and Dinner for the Glaucoma Society will be held on 3 December 2004 at the Royal College of Physicians in Regents Park, London. The meeting will take place between 8.30am and 5pm and the dinner will be held between 6.30pm and 10pm. For further information, please contact: Janet Flowers, Administrator, 29 Quarry Hill, Grays, Essex, RM17 5BT (tel: 01375 383172; e-mail: glauco@uakeire.freeserve.co.uk).

Amsterdam Retina Debate
The Amsterdam Retina Debate will be held on 10 December 2004 at the Academic Medical Centre, Amsterdam, The Netherlands. For further information, please contact: Nicholas Tulp Institute; tel: +31 20 566 8585; fax: +31 20 696 3228; email: retinaidebate@amc.uva.nl

Sunshine Fund for Blind Children
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.

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 Kilimanjaro Centre for Community Ophthalmology (KCCO). 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 particular millions of needlessly blind, The Right to Sight. For further information, please visit www.v2020.org.