



PROGRAMME AND ABSTRACTS

Hosted by:

Belfast Health and Social Care Trust



**Northern Ireland
Regional Medical Physics Service
&
Ophthalmology**

Grand Opera House, Belfast

13-14 September 2010



Welcome

Mo Cháirde - Dear Friends,

A míle uair níos mó ná sé, aon uair a thagann tú as, gídh bé tú, tá fáilte romhat chuig mBéal Feirste le freastal ar an BríSCEV 8 bliantúil.

A thousand times over, wherever you come from, whosoever you be, you are welcome to Belfast for the 8th annual BríSCEV meeting.

Belfast is an industrial city with a history that could be regarded as one of the greatest in the world. At one time it could lay claim not only to the largest shipyard in the world, but also the largest linen mill, tobacco factory and rope works. When the RMS Titanic was launched in 1912, Belfast had become one of the world's most important ports and was extraordinarily wealthy.

During BríSCEV you will have the opportunity to see some of Belfast's impressive architecture; buildings such as Belfast's City Hall and Charles Lanyon's delightful Custom House where the great Victorian novelist Anthony Trollope kept an office. If you look to the east of the city, you will often be able to see Samson and Goliath, the great cranes that built the Titanic. You will visit McHugh's pub, believed to be Belfast's oldest building situated beside the river to service the busy port and hopefully you will have time to visit the Crown liquor saloon, one of the finest examples of a high Victorian public house in existence and now owned by the National Trust.

Although the twentieth century has been a turbulent time for Belfast, our most recent history has once again seen the city transformed, with stylish bars and fine restaurants, world-class hotels and stunning visitor attractions and shopping centres.

We very much hope you enjoy your stay.

Clive Wolsley
Mary Broadbery
George Dempsey
Karen Mahon

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The Travelling Eyes



A UK inter-laboratory standardisation exercise

Contact details: Dr Ruth Hamilton (on behalf of the Board of the British Society for Clinical Electrophysiology of Vision, BriSCEV), Department of Clinical Physics, Royal Hospital for Sick Children, Dalnair Street, Glasgow G3 8SJ. E-mail r.hamilton@clinmed.gla.ac.uk

Dr Hamilton will act as project co-ordinator, and will be responsible for organising visits to co-hosting laboratories, training, preparing standard operating procedures and supplying the photometer. Recruitment of participating labs will be undertaken at the annual meeting of BriSCEV in Belfast, September 2010. Full information will be provided. Labs will require to agree to use of their facilities and to inclusion of findings in data dissemination.

Bank details: c/o Dr Vikki McBain, Treasurer of BriSCEV, v.a.mcbain@abdn.ac.uk

Proposed dates: Multiple visits, October 2010-April 2011

Objectives:

- To record ERGs from the same two adults at every participating UK electrophysiology centre.
- To measure ERG stimuli at each participating UK electrophysiology centre using the same photometer and procedure.
- If stimuli differ from ISCEV standard, to repeat the recording using exact ISCEV standard stimuli if possible.

Aims:

1. To quantify the extent to which ERG stimuli differ across the UK, and from ISCEV standards
2. To quantify the extent of inter- and intra-individual ERG parameter variation (N=2) when using usual routine protocols of participating UK electrophysiology centres.
3. To quantify the extent of inter- and intra-individual ERG parameter variation (N=2) when using exact ISCEV standard protocols in those UK electrophysiology centres.
4. Ultimate aim: to produce standardised UK reference data to ISCEV standard stimuli.

Benefits better diagnostic power - increased UK-wide collaboration - increased feasibility of multi-centre trials involving ERGs – learning experience for the two volunteers.

Description of Research Project and Methods

Background

The benefit to patients of universally applicable reference data is self-evident, whether anatomical¹, psychological² or electrophysiological³. Published and widely accepted reference data provide diagnostic thresholds with a known level of certainty regardless of where a test is conducted. In the absence of such data, it is important that individual laboratories collect normative data⁴, which is a major undertaking, especially in paediatrics.

The UK is a small, but densely populated country with 19 active electrophysiology centres, seeing around 10,000 patients annually. A recent audit of practice showed considerable variability in stated stimuli and in normative ranges for 15 UK labs despite most aiming for ISCEV standard stimuli. As a first step towards UK-

wide reference data, we propose a series of visits by two individuals and a photometer to as many of the UK laboratories as are willing to participate.

Methods

Two volunteers experienced in visual electrophysiology will be recruited. The process will be submitted to UK research ethics committee for multi-site approval. It is proposed to try to include both lightly and strongly pigmented individuals. All UK electrophysiology labs will be invited to participate, and a schedule of travel and series of appointments will be drawn up. Participating labs will be shown the test and calibration protocol ahead of the visit, and the individuals (the “travelling eyes”) will be trained in performing the calibration according to written protocols.

At each lab, all aspects of the routine ERG stimuli will be measured using an IL1700 photometer. Where possible an amplifier check will also be conducted. Should these differ from ISCEV standards, new protocols/settings will be developed which conform exactly to the ISCEV standard (if possible), and resultant stimuli measured as a check. Subjects will be dilated and dark-adapted and have ERGs recorded using the lab’s routine procedure and then again using the exact ISCEV standard stimuli with a standard electrode type. The travelling eyes will then be light-adapted, and have routine and exact ISCEV light-adapted ERGs measured. Records including raw data if available will be kept.

Where possible, two sites can be visited in one day. It is likely that around 12 trips will be necessary to cover the 15 UK labs who contributed to the recent audit of services.

Dissemination

Results will be shared with participating labs, and submitted for publication. They will also be made available on the BriSCEV website.

Time schedule

Volunteers have already been identified, but can be recruited by advertising on the BriSCEV website. It is planned to conduct the visits between October 2010 and April 2011.

¹ Cole TJ, Freeman JV, Preece MA. British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. *Statistics in Medicine* 1998;17:407.

² Wechsler D, Coalson DL, Raiford SE. WAIS-IV. Wechsler Adult Intelligence Scale: Fourth Edition (2008). Technical and interpretative manual. San Antonio, TX: NCS Pearson.

³ Benatar M, Wu J, Peng L. Reference data for commonly used sensory and motor nerve conduction studies. *Muscle Nerve* 2009; 40:772.

⁴ Marmor MF, Fulton AB, Holder GE, Miyake Y, Brigell M, Bach M. Standard for clinical electroretinography (2008 update). *Documenta Ophthalmologica* 2009;118:69–77

Notes

Monday 13th September: 2010 BriSCEV Course
09.00 – 12.00

'Eyes on the Macula' - Assessing Structure and Function with OCT, PERG and Multifocal ERG'

08.30 onwards REGISTRATION

09.00 - 09.05 WELCOME & INTRODUCTION
Lawrence Brown, *Sheffield, UK*
BriSCEV Education and Training Officer

09.05 - 9.50 LECTURE 1 - THE PATTERN ERG AND AUTOFLUORESCENCE IMAGING
Dr Tony Robson, *Moorfields Eye Hospital, London, UK*

9.55 - 10.40 LECTURE 2 - MFERG: INTERPRETATION AND APPLICATION IN CLINICAL PRACTICE
Dr Stuart Parks, *Tennent Institute of Ophthalmology, Glasgow, UK*

10.40 - 11.00 *Coffee Break*

11.00 - 12.00 LECTURE 3 - OCT AND MFERG: COMBINING RETINAL IMAGING AND ELECTROPHYSIOLOGY
Dr Clive Wolsley, *Royal Victoria Hospital, Belfast, UK* &
Dr David Keating, *Tennent Institute of Ophthalmology, Glasgow, UK*

Monday 13th September: BriSCEV Conference

12.00 – 17.30

- 08.30 - 12.00 REGISTRATION
- 12.00 - 13.00 *Lunch and Commercial Exhibition*
- 13.00 - 13.15 WELCOME AND INTRODUCTION
Clive Wolsley, Belfast, UK
- 13.15 - 14.15 GUEST LECTURE: “Genetic Diagnosis Demystified”
Mr Colin *Willoughby*, (Senior Lecturer, Centre for Vision and Vascular Science, Queen's University & Consultant Ophthalmic Surgeon, Royal Victoria Hospital, Belfast)
- 14.15 - 14.25 BriSCEV TRAVELLING EYES: Ruth Hamilton
- 14.30 – 15.00 POSTER PARADE
Moderator: Dorothy Thompson, London, UK
- 15.00 - 15.30 *Afternoon Tea and Commercial Exhibition*
- 15.30 - 16.45 SESSION I: ORAL PRESENTATIONS
Chairperson: Colin Barber, Nottingham, UK
- 16.45 - 17.30 BRISCEV BUSINESS MEETING
- 18.30 - 19.30 WALKING TOUR: Crown Bar to McHugh’s Pub
- 19.30 EVENING FUNCTION: Dinner followed by The O’Malley Experience at McHugh’s Pub

Tuesday 14th September: BriSCEV Conference

9.00 – 15.00

- 9.00 *Introduction*
- 9.00 - 10.15 CASE PRESENTATIONS & ORAL PRESENTATION
Chairperson: Richard Hagan, Liverpool, UK
- 10.15 - 10.45 *Coffee and Exhibition*
- 10.45 - 11.45 GUEST LECTURE: “The Eyes Have It! Ocular Motor Control and Microcirculation
in the Assessment of Neurological and Cardiovascular Disease”
Dr Canice McGivern, (Head of Regional Medical Physics Service, Royal Victoria Hospital,
Belfast)
- 11.45 - 12.15 SESSION II: ORAL PRESENTATIONS
Chairperson:
- 12.15 - 13.30 *Lunch and Commercial Exhibition*
- 13.30 - 15.15 SESSION III: ORAL PRESENTATIONS
Chairperson: David Sculfor, Stoke Mandeville, UK
- 15.15 Conference ends

Notes

Guest Lecture

Genetic Diagnosis Demystified

Mr Colin Willoughby

(Senior Lecturer, Centre for Vision and Vascular Science, Queen's University & Consultant Ophthalmic Surgeon Royal Victoria Hospital, Belfast)

The completion of the Human Genome Project in 2003 was heralded as the dawn of an era of genomic medicine, in which information from genomes would guide clinical decision making and deliver personalized medicine. It was anticipated that accelerated detection of disease-related mutations would improve genetic diagnosis and prognosis. However, delivery of personalized genomic medicine requires not only access to the complete human genetic code, but availability of appropriate genetic tests for individual patients. The genetic heterogeneity of many Mendelian disorders is a major obstacle to obtaining molecular diagnoses in clinical practice. For example, Retinitis Pigmentosa (RP), the commonest inherited retinal degeneration (prevalence 1:4000), is caused by mutations in over 40 genes. Molecular genetic testing is important for clinical care, enabling assignment of risk, genetic counseling and prognosis, and will be essential for enrolling patients in the future gene therapy trials. This talk is aimed at the non-geneticist in order to demystify approaches to determine the genetic basis of inherited retinal disorders. Traditional genetic methods will be explained including linkage analysis, SNP mapping and mutational screening. The field of genetic testing is rapidly changing and new technologies offer significant benefits. I will outline the currently available genetic tests for inherited retinal degeneration in the UK and on a research basis and present the findings of research work using high-throughput gene sequencing undertaken by our group in Queen's University Belfast.

Notes

Monday 13th September

Poster Session 14.30-15.00

CORRELATION BETWEEN MFERG AND MPOD TESTING IN ASSESSMENT OF RETINAL FUNCTION

Emma Berrow (*Birmingham, UK*)

INVESTIGATING THE REPEATABILITY OF SERIAL MFERG IN NORMAL SUBJECTS OVER A PERIOD OF MONTHS

Laura Milner (*Liverpool, UK*)

ELECTRORETINOGRAM MEASURES IN A NORMAL SEPTUAGENARIAN POPULATION

Magella Neveu (*London, UK*)

THE EFFECTS OF REFRACTION ON THE MULTIFOCAL ERG

Rachel Murphy (*London, UK*)

VEP FINDINGS IN CHILDREN WITH SUSPECTED ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM)

Vivien Thorpe (*Glasgow, UK*)

A MULTI-COMPONENT NOISE SOURCE MODEL OF THE ELECTRORETINOGRAM

Tony Fisher (*Liverpool, UK*)

RING FOCAL ERG: A PROPOSAL FOR A SIMPLE SCREENING PROCEDURE FOR AMD

S Williams (*Liverpool, UK*)

CORRELATION BETWEEN MFERG AND MPOD TESTING IN ASSESSMENT OF RETINAL FUNCTION

Emma Berrow, Hannah Bartlett, Frank Eperjesi

Ophthalmic Research Group, School of Life & Health Sciences, Aston University, Birmingham B4 7ET, UK

Purpose: The multifocal electroretinogram (mfERG) [1], is based on a pseudorandom M-sequence stimulation technique that allows simultaneous recording of electroretinograms (ERGs) from many retinal areas at once [2], objectively measuring electrical activity of the cone photoreceptor and bipolar cells. The MPS 9000 macular pigment densitometer employs a subjective technique, heterochromatic flicker photometry, calculating pigment absorption by analysing a subject's judgement of equiluminance from two lights of different colours in the same location in the visual field [3]. It has been shown that macular pigment optical density (MPOD) increases with lutein and zeaxanthin supplementation [4]. It has also been shown that central multifocal electroretinography amplitudes increase with lutein and zeaxanthin supplementation [5]. The aim of this study was to investigate the relationship between central MPOD and central mfERG.

Methods: The study was approved by the Aston University Research Ethics Committee. Central MPOD (0.5 degrees) using the M:POD and central mfERG first order kernel component N1 P1 amplitude (0-2.5 degrees) using the VERIS system was recorded on the eyes of 63 participants aged between 18 and 77 years who all provided written, informed consent. Inclusion criteria were best corrected visual acuity of 6/9.5 (LogMAR 0.2) or better, good central fixation, clear optical media, no signs of retinal or optic nerve disease, good general health and on no medication that affects the retina.

Results: Central MPOD did not correlate significantly with central mfERG amplitude ($r = -0.147$, $p = 0.249$) in this sample. Standard deviation of the MPOD was ± 0.17 (45% of the mean) and for the mfERG P1 amplitude was ± 49.71 (29% of the mean) for both groups combined.

Conclusions: The subjective and objective measures produced by these tests did not correlate. Difference in field sizes between the two measures may account for this, meriting further research.

1. Sutter, E.E. and D. Tran, The Field Topography of Erg Components in Man .1. The Photopic Luminance Response. *Vision Research*, 199; 32(3): 433-446.
2. Sutter, E.E., The Fast M-Transform - a Fast Computation of Cross-Correlations with Binary M-Sequences. *Siam Journal on Computing*, 1991;20(4): 686-694.
3. Bone RA, Landrum JT, Gibert JC. Macular pigment and the edge hypothesis of flicker photometry. *Vision Research*, 2004;44:3045-3051.
4. Richer S, Devenport J, Lang JC. Last ii: Differential temporal responses of macular pigment optical density in patients with atrophic age-related macular degeneration to dietary supplementation with xanthophylls. *Optometry* 2007;78(5):213-9.
5. Parisi V, Tedeschi M, Gallinaro G, Varano M, Saviano S, Piermarocchi S. Carotenoids and antioxidants in age-related maculopathy italian study: Multifocal electroretinogram modifications after 1 year. *Ophthalmology*. 2008 Feb;115(2):324-33 e2.

INVESTIGATING THE REPEATABILITY OF SERIAL MFERG IN NORMAL SUBJECTS OVER A PERIOD OF MONTHS

L.C. Milner, A.Small, R.P.Hagan

Department of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal
Liverpool University Hospital, Liverpool, UK

Purpose: Within the literature it has been well established that the multifocal electroretinogram (mfERG) is a useful clinical tool. However studies assessing the reproducibility of the mfERG are limited. This laboratory has used mfERG as a long-term monitor of anti-VEGF treatment efficacy and also for observing recovery from a variety of retinal diseases. This study aimed to assess the longitudinal reproducibility of the mfERG.

Method: 3 healthy subjects were chosen with normal corrected VA and their mfERG recorded over a 4 month period. Pupils were not dilated and gold foil electrodes were used. A 19 hexagon stimulus was run using a 511 step m-sequence. Four runs were recorded from the right eye and then averaged. The minimum period between measurements was 2 days and the maximum was 1 month. At least 6 runs were obtained from each subject. The average amplitudes and latencies of the P1 and N1 components from each of the concentric rings were analysed to provide a mean and standard deviation allowing the calculation of a coefficient of variation for all the subjects.

Results: The average coefficient of variation of the P1 amplitudes for the 3 subjects was 9.7%, 14.9% and 8.3% for rings 1, 2 and 3 respectively. The average coefficient of variation of the P1 latency was 2.9%, 2.5% and 1.7% for rings 1, 2 and 3 respectively. The average percentage difference between largest and smallest P1 amplitudes recorded for the 3 subjects were 25.8%, 36.4% and 19.4% for rings 1, 2 and 3 respectively. The average percentage differences for P1 latency were 8.0%, 7.5% and 3.8% for rings 1, 2 and 3 respectively.

Conclusion: The mfERG is a suitable tool for the longitudinal evaluation of retinal function. This small study would suggest an increase/decrease in P1 amplitude of 37% from baseline is unlikely to be caused by chance.

ELECTRORETINOGRAM MEASURES IN A NORMAL SEPTUAGENARIAN POPULATION.

Magella M Neveu¹, Alan Dangour², Elizabeth Allen², Anthony G Robson¹, Alan C Bird¹, Graham E Holder¹

¹Electrophysiology Department, Moorfields Eye Hospital, London, UK,

²Nutrition and Public Health Intervention Research Unit, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

Purpose: To report normative electroretinogram (ERG) data in a septuagenarian population.

Methods: Fifty-three healthy subjects between the ages of 70-79 (28 female and 25 male) were examined. All subjects had a full clinical exam and electrophysiological testing. Amplitude and peak time measures were obtained for the ISCEv Standard ERGs, including the “suggested” additional brighter flash ERG. The data are compared with those from a younger group of normal control subjects aged 20-50 years.

Results: The distribution of amplitude and peak time data from all ERG components from all subjects was positively skewed. There was no significant difference between sexes or between eyes for all ERG measures. The amplitude of the bright flash ERG b-wave was approximately 3 times larger than the rod response Erg in older subjects. The amplitude of the cone flicker ERG was approximately two thirds of the single flash ERG b-wave amplitude in the older group. The amplitude of all ERG components in older subjects was approximately 30%-50% smaller than that observed in younger subjects and all components were of longer peak-time. The most variable measure in all subjects was the amplitude of the brighter flash ERG b-wave; the least variable was the peak time of the photopic single flash ERG a-wave.

Conclusion: ERGs in a normal septuagenarian age group show 30-50% lower amplitude than those of a 20-50 year old age group and are of longer peak time. The need adequately to control for age when reporting ERGs is apparent.

THE EFFECTS OF REFRACTION ON THE MULTIFOCAL ERG

Murphy, R; Shihmar, H; Hogg, CR; Neveu, MM ; Holder GE

Electrophysiology Department, Moorfields Eye Hospital, London, UK

Purpose: To investigate the effect of refractive errors on the multifocal ERG (mfERG), and to assess the effect of optical blur on spatial resolution.

Methods: mfERGs were recorded from 6 subjects (23 to 39 years; mean age 27.5 years) using the Retiscan System (Roland Consult). Subject's pupils were dilated with cyclopentolate hydrochloride 1%. MfERG was recorded binocularly using gold foil corneal electrodes and a 61 hexagonal array. The stimulus subtended 57° horizontally. MfERG analysis was performed using 5 concentric rings centered at the fovea. Amplitudes and latencies of p1 and n1 components of the first order kernel were analysed. Each subject was optimally refracted and additional optical blur was introduced in steps of 3 dioptres from -3.00 to +9.00 dioptres (+6.00 and -6.00 dioptres from the optimal of +3.00 dioptres), in a random order. Subjects were also tested with 10 segments of the stimulus array occluded with opaque card to investigate whether the ability to resolve the spatial changes was affected by blur.

Results: Small variations in the amplitude and latency of the p1 component were observed with the use of optical blur. There was an increase in p1 amplitude from primarily the central hexagon (ring 1) with incremental changes in optical correction. The changes in latency of p1 from all rings were between +/-5ms. Similar results were observed in rings 2-5, but to a lesser extent. When specific elements of the stimulus were occluded a proportional loss of amplitude was observed in the responses which corresponded to the occluded hexagons. When using occlusion, p1 amplitude (central hexagon) increased with incremental changes of dioptres and the magnitude of the increase was greater than that without the use of occlusion.

Conclusion: The degree of amplitude variation in response to optical blur/distortion is proportional to the variation in image size at the retina, as described by other authors (Chan and Siu., 2003; Hood et al., 2008). Introducing a large variation (greater than +3.00 dioptres) in refractive error does have a significant impact on signal amplitude. Small variations in optical correction have minimal effect on responses and therefore minimal distortion of the signal; this may be disregarded for most clinical purposes. This will simplify the recording of mfERGs in clinical practice, and also reduce the risk of 'cropping' of the stimulus by the edges of the trial frames and lenses routinely used. When areas of the stimulus were occluded, loss of spatial resolution was not observed with increasing optical blur. This may not be the case where higher resolution arrays or more extensive optical error is present.

VEP FINDINGS IN CHILDREN WITH SUSPECTED ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM)

Vivien Thorpe¹, Michael S. Bradnam^{1,2}, Ruth Hamilton^{1,2}

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²Division of Developmental Medicine, Faculty of Medicine, University of Glasgow, UK

Purpose: To evaluate VEP findings in children referred for electrophysiological assessment with suspected acute disseminated encephalomyelitis (ADEM), an inflammatory, demyelinating condition of the central nervous system which occurs following viral infection or immunisation, has an acute onset with multifocal neurological signs and shows white matter lesions on MRI. In some cases, recurrent episodes fulfil the criteria for diagnosis of multiple sclerosis (MS). Evoked-potential data in this condition is scarce.

Methods: A retrospective audit was conducted of 13 children referred by neurology for VEP assessment because of suspected ADEM. Case Notes and electrophysiology databases were reviewed. Ages at referral ranged from four to 14 years (median eight years). All children were first tested whilst in inpatient care with an episode of neurological abnormality. Electrophysiology included pattern reversal (pr) VEPs for all children. Final diagnosis was determined by the attending neurologist and was based on clinical findings, biochemistry analysis and brain imaging with MRI.

Results: Eight of the 13 children had a final diagnosis of ADEM, two of MS, one of bilateral optic neuritis and one of viral meningitis. Of the eight with a final diagnosis of ADEM, seven demonstrated prVEP abnormalities which included absent responses, delayed responses and/or abnormal morphology. One of the two MS patients had delayed prVEPs at presentation. The optic neuritis patient had markedly delayed prVEPs at presentation and the viral meningitis patient had delayed right and absent left prVEPs at presentation.

Five of the 13 children had serial VEPs, two of whom had ADEM: in both, the VEPs remained delayed despite clinical recovery. Both MS patients had repeat VEPs: the patient with initially delayed VEPs showed gradual normalisation of latency; the other patient continued to show normal VEPs. The optic neuritis patient showed complete recovery of VEP latency two months after the initial assessment.

Conclusions: In seven of the eight children in the current series confirmed with ADEM, the VEP was abnormal during the acute phase, and in both those with serial recordings the VEP remained abnormal despite resolution of symptoms. One of the two MS patients had abnormal VEPs at presentation, which resolved. This audit suggests that prVEPs are an effective means of demonstrating demyelination associated with ADEM and MS in children.

A MULTI-COMPONENT NOISE SOURCE MODEL OF THE ELECTRORETINOGRAM

Fisher A C¹, Hagan R P¹, Brown M C¹, Eleuteri A¹, Lake S P¹, Austin M J¹, Milner L¹, Simpson D M²,

¹Dept. of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool, UK

²Institute of Sound & Vibration Research, University of Southampton, UK

Purpose: To develop a multi-component noise source for the stochastic modelling of the electroretinogram (ERG).

Introduction: The majority of stochastic models of clinical electroretinograms most frequently employ naive noise sources based on simple Gaussian (white) noise. These are of limited use as they are unrealistic and statistically predictable. The lack of realistic noise models continues to hinder progress in developing our understanding and objective characterisation of electrodiagnostic responses. Real-life noise as observed at the electrode/skin interface has, in principle, a number of orthogonal components:

1. DC or 'very low frequency' drift;
2. interface coloured noise;
3. electronic noise;
4. main supply and other (e.g. CRT) 'harmonic' interference;
5. spontaneous discontinuous biological noise (arising from eye movement and muscle-related artefacts);
6. continuous 'biological' noise.

It is proposed that these can be represented statistically as a Brownian (*a.k.a.* $1/f^2$ noise) non-stationary source (Component 1), a pink (*a.k.a.* $1/f$ noise) coloured noise (Components 2 & 3 in combination), a simple combination of sines (Component 4); vector of discontinuous features extracted from *real-life-models* (RLM's) as blind source separable independent components (Component 5), and an auto-regressive generator based also based on an RLM (Component 6).

Methods: A series of algorithms was written in the mathematical language MatLab (Mathworks™). Brownian noise was modelled as the cumulative sum of a series of Gaussian-distributed random numbers with the end-to-end straight line removed. The pink coloured noise was generated in the log frequency/log amplitude space with the Hurst exponent of 0. Sinusoidal noise was modelled as a combination of sines relating to the fundamentals 50 or 60 Hz (for mains interference), 75Hz for CRT interference and their 1st and 2nd harmonics. RLM's were based on a set of 24 *noise-plus-PERG* and 24 *noise-only* recordings made on a Roland RETIsScan/RETIpport instrument using DTL-Plus electrodes. A discrete library of exemplar (non-stochastic) spontaneous noise vectors were extracted from each RLM PERG by Independent Component Analysis (ICA) with synchronous dynamical embedding. The continuous biological noise (no assumption made as to its *colour*) was modelled using an autoregressive (AR) generator. This implementation assumed that the noise process could be realised by a 12th-order all-pole infinite impulse response (IIR) filter driven by Gaussian white noise. Two software graphical user interfaces (GUI's) were developed: a web page written in HTML and JavaScript; and an Excel application. Both acted as clients to software running remotely over the Internet using the Liverpool MatSOAP server environment.

Results: This development provides a realistic approach to the informed graphical noise modelling of the clinical ERG. An infinite series of noise records can be generated with the gain of each component set independently. Template models of the ERG can be scaled and added by simple super-position and form the basis of Monte Carlo-based investigations. This presentation will include a real-time demonstration of this technique and its use in training artificial neural networks for pattern recognition and statistical SNR modelling of the PERG.

Conclusion: This approach provides an environment previously unavailable in electrodiagnostic modelling.

RING FOCAL ERG: A PROPOSAL FOR A SIMPLE SCREENING PROCEDURE FOR AMD

Williams S, Fisher A C, Watt RP, Milner L, Robinson R, Denby CE, Hagan R P

Dept. of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal Liverpool University Hospital and University of Liverpool, Liverpool, UK

Purpose: To implement a highly accessible system of ring focal electroretinography optimised for the screening of AMD.

Introduction: There are presently no screening programmes for AMD. New therapies hold the promise of not just arresting wet AMD but of, in some cases, actually reversing the disease and restoring vision. mfERG has been demonstrated to be useful in assessing the progress and response to treatment of wet AMD in patients who have already experienced visual impairment. However, such an investigation must be regarded as specialised, requiring sophisticated instrumentation, experienced clinical scientific staff and, as such, is limited to relatively few ophthalmology departments. Whilst modern systems of mfERG offer high spatial resolution albeit at the cost of long examination times, it has been shown that low resolution mfERG with the segment stimuli limited to 3 or 4 concentric ring fields has a good SNR capable of characterising the AMD-challenged retina. In principle, screening ring focal ERG can be completed in less than 10 seconds.

Here it is recognised that to deliver an effective ring focal ERG only a modest instrumentation set-up might be required and such a system might be conceivably be engineered to be effectively used in non-specialist centres by non-specialist staff. It is proposed that such a system might form the basis of a cost effective and highly accessible means of AMD screening.

Methods: The ring focal ERG instrument was constructed in prototype form into a portable aluminium 'flight case'. The stimulation element comprises concentric rings of white high-power LED's behind an opalescent Perspex screen. Under local control, the ring stimuli can be represented as:

1. interleaved steady state (29 to 31 Hz);
2. discrete *m-sequence* driven flash transient ERG (~ conventional mfERG) with variable higher-order kernel contributions.
3. discrete flash transient ERG explicitly demultiplexed by Gaussian elimination.

Either silver thread or simple skin electrodes are used. The bioamplifier is a development of the CRS BlueGain Bioamplifier. Control and recording is achieved over a wireless Bluetooth connection from a Laptop PC running a very straight-forward graphical user interface.

Signal processing uses established routines written in MatLab including automatic cursoring and artefact rejection using Principal Component Analysis.

Results: Early results obtained in trials of the prototype have led to the initiation of a project to develop a CE-marked instrument.

Conclusion: The practical implementation of a ring focal ERG Instrument is illustrated. Its potential to support a programme of AMD screening will be evaluated by the BriSCEV and ISCEV communities.

Notes

Notes

Monday 13th September

Scientific Session I

- 15.30-15.45 CORTICAL RESPONSES AFTER ELECTRICAL EPIDURAL STIMULATION OF THE OPTIC NERVE DURING NEUROSURGERY
Mitja Benedicic (*Ljubljana, Slovenia*)
- 15.45- 16.00 MAPPING HAEMODYNAMIC RESPONSES IN THE VISUAL CORTEX TO ISCEV STANDARD CHECKERBOARDS
Uma Shahani (*Glasgow, UK*)
- 16.00-16.15 ISCEV-STANDARD PATTERN REVERSAL VEPS: NORMAL DEVELOPMENT FROM BIRTH TO PUBERTY
Ruth Hamilton (*Glasgow, UK*)
- 16.15-16.30 IS THERE EVIDENCE FOR SLOW, MEDIUM AND FAST TEMPORAL FREQUENCY SUB-SYSTEMS IN LUMINANCE VEPs?
Daphne McCulloch (*Glasgow, UK*)
- 16.30-16.45 INCORPORATION OF A VIDEO SWITCHER/SCALER IN A PATTERN VEP SETUP
Neil Parry (*Manchester, UK*)

CORTICAL RESPONSES AFTER ELECTRICAL EPIDURAL STIMULATION OF THE OPTIC NERVE DURING NEUROSURGERY

Mitja Benedicic, Roman Bosnjak

University Medical Center Ljubljana, Department of Neurosurgery, Ljubljana, Slovenia

Purpose: To present cortical responses after electrical epidural stimulation of the optic nerve (ON) in individuals with normal preoperative vision undergoing surgery for central skull base tumors. Optic nerve evoked potentials (ONEP) after flash and electrical stimulation were additionally recorded.

Methods: Cortical responses were recorded with contact electrodes at Oz with the reference at Fz. Monopolar ONEP were recorded with insulated platinum ball-tipped wire electrode on the surface of ON and an extra-cephalic reference electrode. The distance between stimulating and recording electrodes when recording ONEP after electrical epidural stimulation of ON was 25 mm. Platinum blunt needle electrodes were attached epidurally to both sides of ON when it enters or exits the optic canal and used for electrical stimulation and used to deliver a rectangular current pulse (intensity 0.2 - 5.0 mA; duration 0.1 – 0.3 ms; rate 2 Hz). LED flash goggles were used for flash stimulation through the closed eyelids.

Results: Cortical responses after electrical epidural stimulation of ON consisted of a positive and a negative deflection at 20 ms and 30 ms, respectively, and a smaller positive deflection at 40ms. ONEP after flash stimulation consisted of a positive deflection with a latency around 40 ms, followed by a longer-lasting negativity with the peak at around 50ms. ONEP after electrical epidural stimulation of ON consisted of a negative deflection at around 3 ms.

Conclusions: Stable and repeatable cortical responses after electrical epidural stimulation of ON could safely be recorded in humans during neurosurgery. Further studies are needed to establish their role in intraoperative monitoring of the visual function.

MAPPING HAEMODYNAMIC RESPONSES IN THE VISUAL CORTEX TO ISCEV STANDARD CHECKERBOARDS

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Purpose: To use functional near infrared spectroscopy (fNIRS) to record and localize changes in oxy (HbO) and de-oxyhemoglobin (Hb) concentrations in response to visual stimulation.

Methods: Data were collected on a two-channel oximeter that used the Frequency Domain Multi-Distance (FDMD) method. Stimuli were checkerboards (check width 15 min of arc) presented statically, with phase-reversal or alternated with a grey field of equal mean luminance (ON/OFF) to five healthy subjects (aged 18-25 years) over multiple scalp locations.

Results: Differences between static, phase reversal and ON/OFF checkerboard stimulation were not significant ($p > 0.1$). The largest increases in HbO levels were observed at a distance of 5% to the right and left of the midline occipital location, O_z ($0.84 \pm 0.41 \mu\text{m}$ and $1.07 \pm 0.40 \mu\text{m}$ respectively). The increase in HbO diminished at recording locations over the posterior parietal regions in the vertical direction. Hb changes were substantially smaller than those observed for HbO. Changes in haemodynamic responses as a function of distance indicated the extent of the area of activation of brain tissue as a result of visual stimulation. Longer stimulus presentation times prolonged the time taken to recover to attain baseline measures suggesting that the neurovascular coupling mechanism could be explained by a simple linear relationship.

Conclusion: We have demonstrated that fNIRS can be a useful complementary tool to map visual function in normative and clinical investigations.

ISCEV-STANDARD PATTERN REVERSAL VEPS: NORMAL DEVELOPMENT FROM BIRTH TO PUBERTY

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² Division of Developmental Medicine, Faculty of Medicine, University of Glasgow, UK

Purpose: To describe the changes in ISCEV-standard pattern-reversal VEPs in normal subjects from birth to puberty.

Methods: Infants and children were recruited locally and were tested to ensure normal acuity, eye movements, visual fields, colour and binocular vision and fundal appearance. Black and white checkerboards subtending $25^\circ \times 25^\circ$ with square widths of 60' were presented on a CRT monitor (mean luminance 60 cd/m², contrast 100%) and reversed 2.2 times per second. Attention to the pattern was encouraged with a fixation mark and play (drawing shapes, singing, 'peek-a-boo' etc) as appropriate. Fixation was monitored and data acquisition suspended if the subject looked away. The VEP was recorded between Oz and Fz, with a ground electrode on a mastoid. Reversals were triggered at the top left raster corner. Averaging continued until the VEP was clearly defined, and the recording was repeated to ensure reproducibility. The process was repeated for 15' square widths in co-operative subjects. Reproducible VEPs were averaged and amplitude and implicit time of the P100 was noted.

Results: 60' pattern VEPs were obtained from 169 children, aged from 5 weeks to 15 years. 15' pattern VEPs were obtained from 86 children, aged from 16 weeks to 15 years, and were absent in four children under one. Implicit times of P100 decreased sharply, then more slowly with age. An upper limit of normal (IT(ul)) for 60' and 15' checks could be described using single exponential decay equations (corrected for mid-screen raster trigger) $IT(ul)=110+(250*\exp[-5.5*a])$ (60') and $IT(ul)=120+(60*\exp[-1.2*a])$ (15'), where a is age expressed in years to one decimal place. Amplitudes were far more variable.

Conclusions: These data agree well with findings from other studies, and the equations derived here are applicable to previous work done elsewhere. Laboratories with little or no paediatric normative data, but which are required to test children, might reasonably adopt these equations for normal limits of implicit time, providing due care is taken to match the test methods.

Acknowledgements: The R.S. Macdonald Charitable Trust; The Chief Scientist Office Grant K/RED/4/C279; The Ulverscroft Foundation; Karen Hope and The Nuffield Foundation.

IS THERE EVIDENCE FOR SLOW, MEDIUM AND FAST TEMPORAL FREQUENCY SUB-SYSTEMS IN LUMINANCE VEPs?

Daphne L McCulloch¹, Uma Shahani¹, David S Nicol¹, Taraneh Eliaseh¹, Claire P Allen¹, Ruth Hamilton²

¹Vision Sciences, Glasgow Caledonian University

²Clinical Physics, Royal Hospital for Sick Children and Glasgow University

Purpose: Three distinct temporal frequency sub-systems were defined for steady-state VEPs to luminance flicker in the early days of VEP recording, specifically slow, medium and fast sub-systems at 10 Hz, 16-21 Hz and 40-60 Hz respectively [1]. We have examined VEP frequency-response functions to sinusoidally-modulated full field flicker (FFF-VEPs) to characterize the extent and variability of temporal frequency tuning.

Methods: Binocular and monocular VEPs were elicited in 12 adult volunteers to FFF at ten temporal frequencies ranging from 2.8 to 58.8 Hz. In five additional participants, VEPs were recorded binocularly to 21 flicker frequencies using both red and white flicker and several electrode derivations to replicate early VEP studies. Flicker stimuli were generated by a combination of red, blue and green LEDs integrated in a ganzfeld. Response magnitudes at the stimulus frequency (F1) and at the double harmonic (F2) were analysed.

Results: For both monocular and binocular white flicker the FFF-VEP magnitudes at F1 were maximal for 7.5-10.6 Hz flicker. F2 is maximal for 5.3 Hz. Binocular FFF-VEPs showed a significant medium-frequency peak at 21.3 Hz that was not found in monocular VEP recordings. Binocular testing with more frequencies, and different electrode derivations revealed greater individual variation in the frequency-response functions of the resulting VEPs.

Conclusions: FFF-VEP magnitudes characterized by their frequency-response functions are optimal for 7.5-10 Hz flicker supports the existence of a 'slow sub-system' for both monocular and binocular VEPs. 'Medium frequency sub-systems' (16-22 Hz.) are also evident in binocularly recorded FFF-VEPs. Tuning to an optimal stimulation frequency for high flicker rates was seen in some but not all participants.

[1] Regan D (1975) *Nature* 253:401-407.

INCORPORATION OF A VIDEO SWITCHER/SCALER IN A PATTERN VEP SETUP

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² Diagnosys UK, Cambridge

In paediatric electrophysiology, one of the biggest challenges is to engage and maintain the attention of the child. One approach is to present a video or some other interesting image on the display screen, and interleave or combine this with the test stimulus. Regan (1977) used a video mixer to simultaneously present a low contrast cartoon in combination with a high contrast checkerboard, although care has to be taken in defining contrast of the time-locked stimulus. Many labs use interleaved presentation, interrupting the recording periodically to show a cartoon. An advantage of this is that the child can bring their own favourite video/DVD with them. Often the parent will have bought a new video as a treat (or bribe!) and again this helps co-operation.

This used to be technically straightforward because older, composite video-based systems could simply use a switch to select the source, allowing the transition from cartoon to checkerboard to be practically instantaneous. With the advent of high resolution graphics displays, it is no longer possible to simply switch sources. Even if the cartoon and the visual stimulus have identical video properties, modern graphics monitors black out when they lose sync, and it can take seconds for the new image to appear. In this time the attention of the child can be lost again.

In Manchester we have solved this by using a video switcher/scaler (TV One C2-2255), a device more at home in a TV studio. This can accept and mix several different sources including RGBS, composite video S-video, SDI and HDTV, and these can all have different geometry and timings. It supports picture-in-picture, zooming, keying (showing the secondary source only where the primary is a particular colour), and can present a mixture of the 2 sources or simply swap from one to the other. At present we are currently using the most basic function, swapping from cartoon to stimulus. In order to maintain the original stimulus timing, the output parameters are set to be identical to the original stimulus parameters, and frame synchronization is achieved by enabling genlocking on the scaler. This causes a 2-frame delay between the input and the output, and this is corrected by adding a 22ms trigger delay to the acquisition parameters.

The scaler can be controlled via a serial line and most front-panel functions can be mimicked by a 20-character command send via the RS232 port. We have programmed the acquisition system (Diagnosys E2) to issue these commands at key points so that the VEP procedure starts in DVD mode, and swaps to stimulus when acquisition starts. The device swaps back to DVD on acquisition pause and end. We use an Espion remote control so that the whole procedure can be controlled by the person watching the child's gaze behaviour. Audio can be sent via a separate channel so that this is heard all the time.

The setup has much potential for expansion, enabling us show a composite checkerboard/video (using keying), to use Regan's mixing technique and to have an animated fixation target.

Notes

Notes

Tuesday 14th September

09.00-10.00 CLINICAL CASES

followed by

10.00-10.15 ELECTROPHYSIOLOGY OF CHILDHOOD RETINAL DYSTROPHIES
Malcolm Brown (*Liverpool, UK*)

Notes

ELECTROPHYSIOLOGY OF CHILDHOOD RETINAL DYSTROPHIES

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Purpose: To provide a systematic approach to the diagnosis of causes of impaired vision in childhood with particular reference to the role of electrophysiology in retinal dystrophies.

Methods: We have examined the contribution Electrodiagnostic Testing (EDT) can make in determining, confirming or excluding a diagnosis.

Results: We have set out a systematic approach to diagnosis of both early and late onset disorders, differentiating between retinal and non-retinal causes. Signs, symptoms, inheritance patterns and test results are tabulated against specific disorders showing the contribution EDT can make. Recent example case studies are also presented.

Conclusions: Electrodiagnostic testing is of particular value in identifying and differentiating causes of poor vision where there may not be clear retinal signs in the early stages such as Leber's congenital amaurosis, CSNB, cone dystrophy and albinism. A further role is in the differentiation of retinal from post-retinal causes.

Notes

Guest Lecture

The Eyes Have It!

Ocular Motor Control and Microcirculation in the Assessment of Neurological and Cardiovascular Disease

Dr Canice McGivern

(Head of Regional Medical Physics Service, Royal Victoria Hospital, Belfast)

The eyes present a uniquely versatile and readily accessible site for the non-invasive assessment of a range of diseases and conditions.

Micro-vascular circulations such as those found in the eye have been shown to be preferential sites for the subclinical onset of cardiovascular disease. Alterations in the structure and function of these microcirculations arising from the presence of cardiovascular disease induce changes in blood flow velocity waveforms that supply these microcirculations. Analysis of these blood velocity waveform changes offers the potential of a sensitive and non-invasive quantitative objective method of identifying the onset of cardiovascular disease allowing prompt therapeutic intervention.

The neural pathways that control ocular motor function are well understood and pathology in these structures can be reflected in changes in eye movement function. Analysis of ocular motor function in response to a range of stimuli including reflexive saccades and fixation can be used to provide an objective quantitative assessment of neurological conditions such as multiple sclerosis and Parkinson's disease.

This talk will present an overview of work undertaken in the assessment of cardiovascular disease and neurologically derived movement disorders using the eye as a readily accessible physiological measurement site.

Notes

Scientific Session II

- 11.45-12.00 IN VIVO SAFETY OF TRYPAN BLUE USE IN VITREORETINAL SURGERY
Vikki McBain (*Aberdeen, UK*)
- 12.00-12.15 THE MULTIFOCAL LED STIMULATOR
Sinead Walker (*Glasgow, UK*)

IN VIVO SAFETY OF TRYPAN BLUE USE IN VITREORETINAL SURGERY

Vikki A McBain¹, Ehab A Abdelkader¹, Mrinal Annand¹, Neil W Scott², Rehman M Siddiqui¹,
Noemi Lois¹.

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²Medical Statistics Team, Section of Population Health, University of Aberdeen, UK

Purpose: To evaluate “in vivo” safety of trypan blue (TB) in patients undergoing TB-assisted internal limiting membrane (ILM) or epiretinal membrane (ERM) peeling.

Methods: Prospective study including 21 patients (21 eyes) with full-thickness macular hole (FTMH) and/or ERM undergoing TB-assisted ILM/ERM peeling. Main outcome measures included distance visual acuity (DVA), near visual acuity (NVA), amplitude of P50 and N95 of the pattern electroretinogram and fundus autofluorescence (AF); these were assessed pre-operatively, at 6 (n= 21) and 12 (n= 10) months post-operatively.

Results: There was a statistically significant improvement in DVA, NVA, P50 and N95 amplitude at 6 and 12 months post-operatively. The mean LogMAR DVA and NVA improved from baseline by 0.31 (SD 0.37) and 0.17 (SD 0.31) at 6 months, respectively, and by 0.4 (SD 0.25) and 0.35 (SD 0.28) at 12 months, respectively. The mean P50 and N95 component amplitudes improved by 28% compared to baseline at 6 months (P50 0.4 [SD 0.8]; N95 0.53 [SD 1.07] and by 63% at 12 months (P50 0.9 [0.85]; N95 1.04 [1.34]). AF did not demonstrate damage to the retinal pigment epithelium attributable to TB.

Conclusions: No deleterious effects of TB were observed in this study.

THE MULTIFOCAL LED STIMULATOR

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Purpose: Research into the clinical applications of multifocal ERG has focussed on spatial as opposed to temporal aspects of stimulation due to limitations of current systems. Improved control of temporal characteristics may yield more robust and repeatable multifocal ERG data. This presentation reports the development of a second generation LED stimulator for multifocal ERG which allows high resolution temporal control of the stimulus.

Methods: A multifocal LED stimulator consisting of an array of 61 hexagonal elements scaled with eccentricity was developed. The stimulator utilises 217 isolated, warm white, non-diffused LEDs, one or more located within each stimulus element. Each element is driven by a separate output from a constant current driver source. Integration of a standard USB interface allows control of the multifocal LED stimulator via a PC. The stimulator was developed to provide an open software platform for developers and users.

Results: The multifocal LED stimulator allows simultaneous update of each stimulus element, eliminating problems associated with raster scanning employed by conventional CRT and LCD devices. Independent control of each stimulus element provides allows modulation of local intensity, pulse width and frequency. 128 intensity levels ranging from 0 – 7000 cd m⁻² are available. A pulse width of as short as 1 msec and a switching frequency of greater than 1 kHz may be employed, facilitating high resolution assessment of temporal aspects of retinal processing.

Conclusions: An LED stimulator for multifocal ERG has been successfully developed, facilitating high resolution investigation into temporal characteristics of retinal processing. Improved understanding of temporal aspects of retinal function may allow development of multifocal ERG protocols tailored to investigate specific disease states. The modular open control software of the multifocal LED stimulator allows integration with existing and new electrophysiology systems. This may allow standardisation of multifocal ERG, which may help broaden the use of the technique in multi-centre evaluations of new surgical and pharmacological interventions for disorders with retinal involvement.

NOTES

Tuesday 14th September

Scientific Session III

- 13.30-13.45 THE SECOND LIMB OF THE B-WAVE AMPLITUDE–ENERGY RELATION: AN INTERPRETATION.
John Robson (*Houston, USA*)
- 13.45-14.00 A MULTI-CENTRE TRIAL OF FLICKER ERG INTER-STIMULUS INTERVAL MEASUREMENT
Michael Bradnam (*Glasgow, UK*)
- 14.00-14.15 MAGNITUDE SQUARED COHERENCE AND BOOTSTRAP AS OBJECTIVE MEASURES OF PRESENT: NOT-PRESENT RESPONSES IN THE ELECTRORETINOGRAM
Antony Fisher (*Liverpool, UK*)
- 14.15- 14.25 *Comfort break*
- 14.25-14.40 3 MONTH FOLLOW UP OF AMD PATIENTS TREATED WITH LUCENTIS USING MFERG
Richard Hagan (*Liverpool, UK*)
- 14.40-14.55 DESFERRIOXAMINE RETINAL TOXICITY: A CASE STUDY.
Anne Georgiou (*London, UK*)
- 14.55-15.10 LONGITUDINAL IMAGING AND STRUCTURE-FUNCTION CORRELATES OF HIGH DENSITY RINGS OF FUNDUS AUTOFLUORESCENCE IN RETINITIS PIGMENTOSA.
Anthony Robson (*London, UK*)
- 15.10 LIFE, THE UNIVERSE AND EVERYTHING
Malcolm Brown (*Liverpool, UK*)

THE SECOND LIMB OF THE B-WAVE AMPLITUDE–ENERGY RELATION: AN INTERPRETATION.

John Robson

University of Houston College of Optometry

Purpose: to establish the origin of the second limb of the b-wave amplitude–energy relation prior to defining a curve-fitting procedure to be proposed as part of an extended ISCEV protocol (#11. Rod b-wave series)

Background: it is generally believed that the dark-adapted ganzfeld flash ERG is the sum of a transient positive-going signal from rod bipolar cells (PII) and a negative-going signal from rods that rises monotonically to a plateau level that may be maintained for some time prior to its return to baseline. In this context it is normally supposed that the timecourse of the rod contribution to the ERG is the same as that of the photocurrent generated by the outer-segments of rods as recorded from electrically isolated rod outer segments in vitro. We now suggest that these assumptions are not completely correct and a more exact analysis of the mechanism involved in generating the direct rod component of the ERG is required for a full understanding of the amplitude–energy relation of both a- and b-waves.

Result: Simulation of the ERG flash response using the known electrical properties of mammalian rods and their axons (Hagins et al 1970) indicates that the rod contribution to the recorded ERG a-wave evoked by strong stimuli will have, in addition to a component having the timecourse of the outer-segment photocurrent, 1) an initial fast “nose” reflecting the transient current that flows to charge the capacitance of the membranes of rod axon and soma as well as 2) a slower “nose” reflecting a delayed recovery of the membrane voltage of the rod inner segment resulting from hyperpolarisation-induced changes in membrane conductance.

The total duration of the transient nose voltage is less than the time to peak of the bipolar-cell signal (PII) and hence the b-wave amplitude is to a first approximation obtained by summing (algebraically) the peak amplitude of the nose with that of PII and the amplitude of the sustained component of the rod contribution at the time of the PII peak.

Conclusion: the second limb of the b-wave amplitude–energy relation is primarily a reflection of the contribution of the a-wave “nose” to the ERG and this should be taken into account in devising the mathematical model specified for fitting measurements of b-wave amplitude obtained with a series of different energies.

A MULTI-CENTRE TRIAL OF FLICKER ERG INTER-STIMULUS INTERVAL MEASUREMENT

Michael S Bradnam^{1,2}, Richard G Boulton^{1,2}, Ruth Hamilton^{1,2}, Donald C Smith¹

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Purpose: The 30 Hz flicker ERG can be objectively analysed in the frequency domain, giving optimal signal-to-noise ratio, if the inter-stimulus interval is known precisely. Calibration of flicker inter-stimulus interval may provide more information than manufacturer's data. To maximize the signal-to-noise ratio in the frequency domain, it is necessary for the data epoch to include at least ten stimulus cycles and for there to be a maximum inter-trial variability of +/- 0.12 stimulus cycles. The study had three aims:

1. To determine the period and variability of measured inter-stimulus intervals for flicker ERGs from electrophysiology systems in different laboratories.
2. To determine the feasibility of objective flicker ERG measurement with existing instruments.
3. To test the logistics and feasibility of making calibration measurements in a number of laboratories using a shared test instrument.

Methods: Eighteen centres within the UK were contacted via the members' page of the BriSCEV website. A simple battery-powered instrument was developed to measure the inter-stimulus interval of flicker ERG stimuli with a resolution of 10 μ s. Three identical instruments were produced and were circulated over a period of eight weeks with instructions sent and results returned by email. Users were asked to run their electrophysiology system as per clinical routine for flicker ERGs and to measure the inter-stimulus interval at the centre of the stimulus. To assess inter-trial variability, measurements were made five times. To assess suitability for frequency domain analysis, routine recording epoch and sampling frequency were also requested. Results were anonymised, analysed and shared with the participating centres.

Results: All 18 centres agreed to take part and returned results. Measurements typically took less than one hour to record with normal turn-around times being one week. Data were returned for 31 electrophysiology systems. Inter-stimulus intervals were stable (zero variability) for 24 of the 31 systems. Five systems showed marginal variability (≤ 0.04 ms between measurements) and two, where the stimulus externally triggered the recording system, had variabilities of 0.85 and 1.12ms. Median inter-stimulus intervals ranged from 33.00 to 35.00ms. Epochs ranged from 100 to 1024ms; and sampling frequencies from 1,000 to 20,000Hz. The resultant number of data points per epoch ranged from 100 to 2,000. Four systems had stimulus and recording protocols that were suitable for frequency domain analysis. A further 25 systems could, in future, make use of frequency domain analysis if the recording epoch were increased to include a minimum of 10 stimulus cycles. The remaining two systems would be suitable for frequency domain analysis if the inter-trial variability of the inter-stimulus interval could be reduced.

Conclusions: Equipment calibration is required by ISCEV guidelines, but can be time-consuming and technically challenging. This study has demonstrated the feasibility of calibrations across laboratories using a simple instrument circulated by mail. With minor changes to protocols, frequency analysis could be applied in most cases but flicker variability would need to be overcome in some systems with external triggering. It was encouraging that all centres were keen to participate and this would suggest that the strategy of calibrating visual electrophysiology equipment by means of simple shared instruments could be successful.

Acknowledgements: Karen Bradshaw, George Brimlow, Lawrence Brown, Brian Cater, Charles Cottrill, Richard Hagan, Chris Hogg, Vikki McBain, Angela McCall, Daphne McCulloch, Katie Mortlock, Rachel North, Neil Parry, Madeline Perry, David Sculfor, Paul Spry, Jo Steen, Dorothy Thompson, Yaqin Wen, Clive Wolsley.

MAGNITUDE SQUARED COHERENCE AND BOOTSTRAP AS OBJECTIVE MEASURES OF PRESENT: NOT-PRESENT RESPONSES IN THE ELECTRORETINOGRAM

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Purpose: To describe the theory and practical implementation on clinical instruments of 2 statistical tests to demonstrate objectively the presence or absence of a response in the electroretinogram (ERG) at arbitrary *signal-to-noise* (SNR) ratios.

Introduction: Presently, no clinical instrument presents an objective statistic for the presence of a biological response in the ERG. The *human expert* (The Clinician) has no means of knowing if the response, as inferred from the ensemble average, is a *bone fide* estimation of an underlying biological response or simply a manifestation of random noise. The risk here is that an aberrant waveform response will be erroneously characterised by conventional cursoring of its local amplitude maxima and minima without any justification. There is no estimate of confidence level to minimise this risk. However, two recent developments in applicable mathematics now provide simple and conventional *p values* to resolve this issue and are demonstrated here to be straight-forward to apply in clinical practice. The Bootstrap Test (time domain) is arithmetically trivial to perform but is limited by the requirement for the data record to be time-continuous which is not available on the majority of clinical instruments. Conversely, the Magnitude Squared Coherence (MSC) Test (frequency domain), whilst mathematically more complex, can operate on segmented *epoch-by-epoch* data. Both methods produce a robust *p value* for the null hypothesis of no response signal present. The Pattern Reversal ERG (PERG) is used here, but methods are equally applicable to all visual evoked responses.

Methods: The Bootstrap and MSC algorithms were written in the mathematical language MatLab (Mathworks™, Cambs., UK) and located on an Internet-accessible web server running the Liverpool MatSOAP environment. These implementations were designed to be directly available to The Clinician both as a single web page via a simple browser or as an Excel™ spreadsheet application.

Both tests were validated against synthetic stochastic PERG records based on auto-regressive (AR) models constructed from 24 *noise-plus-PERG* and 24 *noise-only* recordings made on a Roland RETIscan/RETIport instrument using DTL-Plus electrodes. In a series of Monte Carlo realisations, numerical experimental *p values* for the no signal *null hypothesis* were compared to those predicted by theory. Continuous and discontinuous data records were used for the Bootstrap and MSC tests respectively.

Results: Very high levels of agreement ($p < 0.001$) between theory and experiment were found for Bootstrap and MSC models across an extensive range of SNR's [0...-40dB]. No difference ($p < 0.01$) was demonstrated for the accuracy of either model at any SNR. Implementations via web-page browser or Excel required no particular mathematical expertise and performed identically.

Conclusion: Both the Bootstrap and MSC Tests for testing the *present: not-present* response in the MSC provide an unequivocal *p value* and perform identically. The MSC has the advantage that it can be applied directly to the segmented recordings available on all clinical instruments.

3 MONTH FOLLOW UP OF AMD PATIENTS TREATED WITH LUCENTIS USING MFERG

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Purpose: To evaluate changes in the multifocal electroretinogram (mf-ERG) in patients with neovascular age-related macular degeneration (nAMD) undergoing ranibizumab treatment.

Methods: Observational longitudinal prospective study. Treatment-naive patients with nAMD meeting inclusion and exclusion criteria. Patients had mfERG recordings at baseline, 1, 4 and 12 week follow up. Best corrected visual acuity (BCVA) were carried out at baseline and week 12 along with a reduced vision protocol and optical coherence tomography (OCT) at baseline and weeks 4, 8 & 12.

Results: Eighteen patients were enrolled. Between baseline and week 12 median BCVA improved from 59 to 69 ETDRS letters ($p=0.001$), mean central foveal thickness (CFT) with OCT decreased from 294 to 199 μm ($p=0.005$), mean P1 amplitude density of the central ring of mf-ERG increased from 35.85 to 51.55 nV/deg^2 ($p=0.009$). mf-ERG response showed correlation both with visual acuity (F-statistic 22, p-value 0.00002) and CFT (F-statistic 12.73, p-value 0.00078).

Conclusion: Intravitreal ranibizumab has proven to be a successful treatment for some patients, with a significant improvement in mean BCVA, an increase in mean mfERG central hexagon amplitude and reduction in mean central retinal thickness followed up over three months. A longer follow up is warranted to assess the long term effects of the drug.

DESFERRIOXAMINE RETINAL TOXICITY: A CASE STUDY

Georgiou AL, Burton LC, Campbell R, Egan C, Holder GE
Moorfields Eye Hospital, London, UK

Purpose: To describe the clinical and electrophysiological features in a patient with presumed acute desferrioxamine toxicity who presented with a sudden loss of vision in the right eye.

Methods: The patient was tested using pattern and full field ERGs which were performed to international standards using gold foil recording electrodes. They also underwent relevant clinical assessments including fluorescein angiography, autofluorescence imaging and OCT.

Results: There was a marked asymmetry between the eyes with the right eye showing a more severe dysfunction than the left.

Right eye results: The PERG was undetectable. Rod specific ERGs were undetectable and bright flash dark adapted ERGs showed a severe reduction with the b-wave more affected than the a-wave. Photopic 30Hz flicker ERG was delayed and of subnormal amplitude and the single flash photopic ERG showed only a residual and delayed response.

Left eye results: The PERG showed possible residual activity both at standard distance and with a large field stimulus. The rod specific ERG was reduced below normal levels, however the bright flash dark adapted ERG was less affected with only a mildly subnormal a-wave being seen. 30Hz flicker ERG was of normal amplitude but with a delay and single flash photopic ERG showed a slight reduction in amplitude of the b-wave which was delayed.

Due to these results the patient was taken off desferrioxamine and returned for repeat testing 4 months later. At this time there was an improvement of the PERG in both eyes and the full field ERG also showed some improvements in both eyes under scotopic and photopic conditions.

Conclusion: The results show the value of electrophysiological monitoring in this patient with presumed desferrioxamine toxicity. The recovery of function following cessation of the drug has been previously described but the novel imaging findings have not previously been reported.

LONGITUDINAL IMAGING AND STRUCTURE-FUNCTION CORRELATES OF HIGH DENSITY RINGS OF FUNDUS AUTOFLUORESCENCE IN RETINITIS PIGMENTOSA

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Purpose: To examine the evolution, functional and structural significance of parafoveal rings of high density fundus autofluorescence (AF) in patients with retinitis pigmentosa and preserved visual acuity.

Methods: Fifty two patients with retinitis pigmentosa or Usher syndrome were ascertained who had a parafoveal ring of high density AF and a visual acuity of 6/9 or better. All had International-standard full-field and pattern ERGs (PERG). Thirty had repeat AF imaging after periods of up to 9 years. Thirty five of 50 underwent ocular coherence tomography (OCT).

Results: Progressive ring constriction was detected in 17 cases. Ring radius reduction varied between 2.9 and 40.4% at a mean rate of between 0.8 and 15.8% per year. There was high correspondence between the width of preserved OCT IS/OS lamina and ring width along the same OCT scan plane (Slope=0.9, $r=0.97$, $p<0.005$, $N=35$) and between preserved IS/OS lamina and pattern ERG P50 ($R=0.72$, $P<0.005$, $N=34$).

Conclusions: Rings of increased AF surround areas of preserved outer retina and preserved photopic macular function. Serial AF images may be a useful prognostic aid providing that the rate and linearity of ring constriction is established. Ring size and rate of constriction are likely to prove important in attempts to identify retinal areas amenable to functional rescue and will assist in the identification of candidates suitable for therapeutic intervention.

LIFE, THE UNIVERSE AND EVERYTHING

Malcolm Brown

**Medical Physics and Clinical Engineering Dept., Royal Liverpool University Hospital, Liverpool L7
8XP, UK**

This talk will cover new thinking on colour vision and other things such as why we humans have very poor sense of smell, and hardly respond to pheromones at all. However, being the last talk of the conference, it will not be too intellectually demanding, nor too serious if missed.

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Monday 13th September: BriSCEV Conference

12.00 – 17.30

08.30 - 12.00	REGISTRATION
12.00 - 13.00	<i>Lunch and Commercial Exhibition</i>
13.00 - 13.15	WELCOME
13.15 - 14.15	GUEST LECTURE: "Genetic Diagnosis Demystified"
14.15 - 14.25	BriSCEV TRAVELLING EYES
14.30 – 15.00	POSTER PARADE
15.00 - 15.30	<i>Afternoon Tea and Commercial Exhibition</i>
15.30 - 16.45	SESSION I: ORAL PRESENTATIONS
16.45 - 17.30	BRISCEV BUSINESS MEETING
18.30 - 19.30	WALKING TOUR
19.30	EVENING FUNCTION: Dinner & The O'Malley Experience at McHugh's Pub

Tuesday 14th September: BriSCEV Conference

9.00 – 15.00

9.00 - 10.15	CASE PRESENTATIONS AND ORAL PRESENTATION
10.15 - 10.45	<i>Coffee and Commercial Exhibition</i>
10.45 - 11.45	GUEST LECTURE: "The Eyes Have It!"
11.45 - 12.15	SESSION II: ORAL PRESENTATIONS
12.15 - 13.30	<i>Lunch and Commercial Exhibition</i>
13.30 - 15.15	SESSION III: ORAL PRESENTATIONS
15.15	<i>Conference ends</i>