British Society for Clinical Electrophysiology of Vision

7th Annual Meeting

Hosted by:

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Medical Physics & Clinical Engineering
&
Ophthalmology

at

Sheffield Hallam University
City Campus

14th & 15th September 2009

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Welcome

Dear Friends,

We are delighted to welcome you to Sheffield for the 7th BriSCEV National Meeting. With a population of over half-a-million, Sheffield is Britain's fourth largest city. It is also the greenest: with one third of it residing in the Peak District National park, it has more trees per person than any other city in Europe!

Despite what you may have seen in the film 'The Full Monty', Sheffield's economy has undergone a strong revival, with Hallam noted to be the richest district outside London. Not only is the city home to two leading universities: The University of Sheffield, and Sheffield Hallam University, it has two professional football teams: Sheffield Wednesday and Sheffield United. It is also home to the world's oldest and second oldest Association football clubs: Sheffield FC and Hallam FC; the latter still play at Sandygate, which is the oldest football ground in the world!

It is of course innovative and specialist steels for which Sheffield is most famous, including crucible steel, which was invented here in 1740, and stainless steel which was first industrialised in 1912. Other stainless steels contemporaneously developed in Germany and the USA are not as good. In addition to producing the best cutlery, Sheffield still leads the world in cast and forged products, so it is appropriate then that the BriSCEV 2009 logo should be Vulcan, the god of smelting, who can be seen atop Sheffield Town Hall. With the city's industrial sector astutely located to the North-East, our smoke and fumes drift over Rotherham, leaving Sheffielders to enjoy clean fresh air from the Pennines!

According to lore, Sheffield is built on seven hills, although OS maps seem to show eight! It is between these hills in the picturesque wooded valleys, perhaps most notably Abbeydale and Rivelin, that fascinating relics of our industrial past are to be found, often hidden by undergrowth, where water from our seven rivers once powered the early forge hammers and grinding wheels.

We do hope that you enjoy your stay here, and that you will have the opportunity to appreciate the city and its stunning environs.

Lawrence Brown
Jamie Healey
Louise Heath
Lindsey Hughes
Lynne Rossiter
Brigitte Kaviani

We would like to thank all our sponsors for their generous support. Please take time to meet them during the exhibition and whenever you have a spare moment. Their contribution helps to keep the cost of your meeting down!

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Participant List

Saed	Abdlseaed	Glasgow Caledonian University
Laude	Augustinus	Princess Alexandra Eye Pavilion, Edinburgh
Colin	Barber	Queens Medical Centre
Debra	Beer	Queens Medical Centre
Alison	Binns	Cardiff University
Karen	Bradshaw	Royal Victoria Infirmary, Newcastle
Lawrence	Brown	STH - organiser
Sarah	Brown	Orthoptics Department, Oxford Radcliffe Hospital
Malcolm	Brown	Medical Physics and Clinical Engineering, Royal Liverpool
Andrew	Carter	Moorfields Eye Hospital
Brian	Cater	Royal Victoria Hospital, Newcastle
Charles	Cottriall	Optometry Department, Oxford Eye hospital
Kong Y	Chin	Medical Physics Department, Leicester
Degg	Christopher	Medical Physics , Leicester
Christine	Denby	Royal Liverpool University Hospital
Anthony	Fisher	Royal Liverpool University Hospital
Marÿke	Fox	Queens Medical Centre
Allannah	Gaffney	Cardiff University
Richard	Hagan	Royal Liverpool University Hospital
Elizabeth	Halley	Moorfields Eye Hospital
Sam	Hayton	Birmingham Childrens' Hospital
Jamie	Healey	STH - organiser
Tony	Hermens	University of Nijmegen St. Radboud
Elisabeth	Hoeks	University of Nijmegen St. Radboud
Chris	Hogg	Moorfields Eye Hospital
Lindsey	Hughes	STH - organiser
Kathryn	Jenkins	Arrowe Park Hospital
Tony	Johnston	Aberdeen Royal Infirmary
Anni	Jowett	Queens Medical Centre
David	Keating	Gartnavel General Hospital
Susanne	Kelly	Stoke Mandeville
C S	Lim	Queens Medical Centre
Ruth	Lyons	Great Ormond Street
Caroline	May	Sunderland Royal Hospital
Vikki	McBain	Aberdeen Royal Infirmary
Angela	McCall	Gartnavel hospital
Ann	McQuiston	Gartnavel General Hospital
Tessa	Mellow	Great Ormond Street, London
Laura	Milner	Royal Liverpool University Hospital
Ray	Mitchell	Unimed
Rachel	North	Cardiff University
Stuart	Parks	Gartnavel General Hospital
Madeline	Perry	Bristol Eye Hospital
John	Robson	University of Houston College, Cambridge
Anthony	Robson	Moorfield Eye Hospital

Richard	Robson	Diagnosys
Lynne	Rossiter	STH - organiser
Gillian	Rudduck	Wirral University Teaching Hospital
David	Sculfor	Buckingham Hospital
Anne	Small	Royal Liverpool University Hospital
Paul	Spry	Bristol Eye Hospital
Jo	Steen	Optometry Department, Oxford Eye hospital
Paul	Taylor	Scottish Health innovations
Dorothy	Thompson	Great Ormond Street
Sinead	Walker	Gartnavel General Hospital
Sharon	Wallace	Queens Medical Centre
Yaqin	Wen	Queens Medical Centre
Amanda	Westerman	Doncaster & Bassetlaw
Clive	Wolsley	Royal Victoria Hospital, Northern Ireland
Ashley	Wood	Cardiff University

Sunday 13th September

18:00 - 19:30 **BriSCEV Officers' Meeting** Strada Restaurant, Leopold Square, Sheffield City Centre

19:30 for 20:00 **Early Arrivers' meal** Strada Restaurant, Leopold Square, Sheffield City Centre

Monday 14th September

8:00 onwards Registration and Coffee
Posters up

08:30 - 11:45 The BriSCEV Course

08:30 - 10:00 Part 1 Calibration
08:30 - 09:15 **Essentials of Photometry for Clinical Electrophysiology of Vision** - Daphne McCulloch
09:15 - 10:00 **Electronics and Signal Processing** - Chris Hogg

10:00 - 10:15 Coffee

10:15 - 11:45 Part 2 Normative Data
10:15 - 11:00 **Variability of Results** - Malcolm Brown
11:00 - 11:45 **Statistics & Data Analysis** - Tony Fisher

11:45 - 12:45 **Buffet Lunch and Commercial Exhibition**
12:00 - 12:45 **Clinical Case Presentations** Chair TBC

12:50 - 13:00 **Welcome & Introduction**
Lawrence Brown, Royal Hallamshire Hospital

13:00 - 16:30 **Session 1 Science Programme** **Chair: Colin Barber**

13:00 - 14:00 **Guest Lecture**
Electromagnetic Field Effects - from Transcranial Magnetic Stimulation to Possible Hazards of Mobile Phones and Powerlines
Professor A. T . Barker
Medical Physics, Royal Hallamshire Hospital, Sheffield

14:00 - 15:15 Oral presentations x 4

14:00 - 14:15 **Evaluation of the Intensity-Response Series of the Focal Rod ERG**
Ashley Wood, Alison Binns, & Tom Margrain
School of Optometry and Vision Science, Cardiff University, UK

14:15 - 14:30 **L- and M-cone isolating ERGs using silent substitution: comparison of CRT and LED devices**
Neil Parry[1], Jan Kremers[2], Ian Murray[3], Declan McKeefry[3] and Naveen Challa[4]
(1) Vision Science Centre, Manchester Royal Eye Hospital
(2) University Eye Clinic, Erlangen, Germany
(3) Faculty of Life Sciences, University of Manchester
(4) Dept of Optometry, University of Bradford

14:30 - 14:45 **Do measured ERG stimulus parameters determine the response, or are there other factors at work?**

M.C. Brown*, R.F. Lowson, R.P. Hagan, A. Small, A.C. Fisher
Medical Physics and Clinical Engineering Dept. & Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool
**email: EDT@MalcolmBrown.com*

14:45 - 15:00 **Explicit Detection of PERG above Noise Floor allows for Early Stopping of Recording**
L.C. Milner[1], A.C. Fisher[1], M.J. Austin[1], A. Small[1], R.P. Hagan[1], M.C. Brown[1], S.P. Harding[1], D.Simpson[2]
(1) Department of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool
(2) UK Institute of Sound & Vibration Research, University of Southampton, UK*

15:00 - 15:15 **Setting Confidence Limits to Automatically-Generated Cursor Positions: A Simple Statistical Approach**
A.C.Fisher[1], M.J.Austin[1], L.Milner[1], M.C.Brown[1], R.P.Hagan[1], S.P.Harding[1], D.Simpson[2]
(1) Department of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool, UK
(2) Institute of Sound & Vibration Research, University of Southampton*

15:15 - 15:30 **Poster Parade** Moderator: TBC

15:30 - 16:15 **Afternoon Tea, Posters and Commercial Exhibition**

16:45 **1st Party leaves for The Sheffield Wheel (those not attending the BriSCEV business meeting)**

16:45 - 17:45 **BriSCEV Business Meeting**

17:45 **2nd Party leaves for The Sheffield Wheel**

19:30 - 23:30 **Dinner and Entertainment at Cutlers' Hall**

Tuesday 15th September

08:45 - 09:10 Registration and coffee

09:10–09:15 **Welcome**
Jamie Healey, Royal Hallamshire Hospital

09:15 - 10:15 **Session 2 Science programme** **Chair: David Keating**

Nitty-Gritty
09:15 - 09:30 **Refraction**: Jon Whittle - Royal Hallamshire Hospital, Sheffield
09:30 - 09:55 **A Guide to Nystagmus**: Helen Griffiths - Royal Hallamshire Hospital, Sheffield
09:55 - 10:10 **Getting the most from your Ganzfeld** : Chris Hogg - Moorfields Eye Hospital, London

10:15 - 10:45 **Coffee and Exhibition**

10:45 - 11:45 **Guest Lecture**
Ocular Tumours
Professor I G Rennie - The University of Sheffield

11:45 - 12:00 **Oral presentation** x 1
The timecourse of single-photon signals in the dark-adapted retina
J.G. Robson and L.J. Frishman
University of Houston College of Optometry

12:00 - 13:00 **Buffet Lunch**

13:00 - 15:45 **Session 3 Science programme**

13:00 - 14:15 **Oral presentations x 5** **Chair: Tony Fisher**:

13:00 - 13:15 **ERG findings in patients with a K+ channelopathy due to a mutation in KCJN10 gene** *(Presented at ISCEV 2009)*
D.A. Thompson[1], R. Kleta[1], S. Feather[2], H. C. Stanescu[1], A. A. Zdebik[1], W. van't Hoff[1], I. Russell-Eggitt[1], A. Dobbie[2], R. Warth[3], E. Sheridan[2], D. Bockenhauer[1]
(*(1) Great Ormond Street Hospital / University College London, London, UK*
(2) Leeds Teaching Hospitals / University of Leeds, Leeds, UK
(3) Physiology, University of Regensburg, Regensburg, Germany

13:15 - 13:30 **Phenotypic assessment of autosomal recessive Congenital Stationary Night Blindness with and without mutations in GRM6**
A.G. Robson[1 2], P. Sergouniotis[2], Z. Li[2], A.T. Moore[1 2], G.E. Holder[1 2], A.R. Webster[1 2]
(1) Moorfields Eye Hospital, 162 City Road, London
(2) UCL Inst. Of Ophthalmology, Bath Street, London

13:30 - 13:45 **Optimisation of Signal Quality During Multimodal Imaging using Combined OCT/SLO and Micro-Multifocal ERG**
S. M. Walker, S. Parks, D. Keating
ElectroDiagnostic Imaging Unit, Tennent Institute of Ophthalmology, Gartnavel General Hospital, Glasgow

13:45 - 14:00 **Comparing localised retinal function from mfERG with estimates of cone density from in vivo imaging of the photoreceptor mosaic using a modified Heidelberg Retina Tomograph**
C.J. Wolsley[1 4], A. Turpin[3], P.J. Morrow[3], B. Scotney[3], R.S. Anderson[1 2]
(1) Vision Science Research Group, School of Biomedical Sciences, University of Ulster, Coleraine, N.Ireland UK
(2) Moorfields Eye Hospital/UCL Institute of Ophthalmology, London, UK
(3) School of Computing and Information Engineering, University of Ulster, Coleraine, N.Ireland UK
(4) Medical Physics, Royal Victoria Hospital, Belfast, UK

14:00 - 14:15 **Ocular pigmentation in light- and dark- adapted ERGs**
Abdlseaed A Al[1], McTaggart Y[1], Ramage T[1], Hamilton R[2], McCulloch DL[1]
(1) Glasgow Caledonian University, Glasgow, UK
(2) Departments of Clinical Physics, Royal Hospital for Sick Children and University of Glasgow, Glasgow, UK

14:15 - 14:45 **Afternoon Tea, Posters and Exhibition**

14:45 - 15:45 **Oral presentations x4** **Chair: Charles Cottriall**

14:45 - 15:00 **Asymmetries in evoked potentials in children...what do they mean?**
Tessa Mellow, Alki Liasis, Ruth Lyons, Dorothy Thompson
Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children, London

15:00 - 15:15 **Relationship between VEP Trans-Occipital Asymmetries and Structural Changes identified by MRI**
Ruth Lyons, Alki Liasis, Tessa Mellow, Dorothy Thompson
Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital, London, UK

15:15 - 15:30 **The Step VEP Acuity Test in Suspected Functional Visual Acuity Loss**
Ruth Hamilton[1], Michael S Bradnam[1], Gordon N Dutton[2]
(1) Departments of Clinical Physics, Royal Hospital for Sick Children and University of Glasgow
(2) Department of Ophthalmology, Royal Hospital for Sick Children, Glasgow

15:30 - 15:45 **Light Pipes in the Retina**
Malcolm Brown
Medical Physics and Clinical Engineering Dept., Royal Liverpool University Hospital

15:45 - 16:00 **Closing remarks and Prize giving**

16:00 **Meeting ends**
Certificates of attendance issued

Seventh Annual Business Meeting

Monday 21st September 2009

16.45 - 17.45

Agenda

1. Opening by the Chairman

2. Minutes of the 2008 meeting held in Cardiff

3. Report of the Chairman

4. Report of the Secretary

5. Report of the Treasurer

6. Report of the Education Officer

7. Elections

8. Future meetings

Monday 14th September

13:00 – 14:00

Guest Lecture

Electromagnetic Field Effects - from Transcranial Magnetic Stimulation to Possible Hazards of Mobile Phones and Powerlines

Professor A. T. Barker

Medical Physics, Royal Hallamshire Hospital, Sheffield

We are all exposed, on a daily basis, to electromagnetic fields from a variety of sources. Some of these exposures are intentional; others are an indirect consequence of a range of technologies.

One intentional exposure uses large pulses of magnetic field to stimulate nerves and the human brain, by inducing currents in the body. In the twenty-four years since its first practical demonstration transcranial magnetic nerve stimulation (TMS) has become widely used in neurophysiology, psychology and psychiatry as well as other disciplines. This talk gives a brief introduction to the principles, early development and state-of-the-art of this readily demonstrable application of an electromagnetic field.

More controversial is our inadvertent exposure to fields from sources such as mobile phones and overhead power cables. There is much public concern, and scientific debate, over possible health risks from such fields. The sources and magnitudes of these fields will be discussed, along with some of the key findings from the literature, to act as an introduction to this controversial area.

14:00 - 14:15

Evaluation of the Intensity-Response Series of the Focal Rod ERG

Ashley Wood, Alison Binns, & Tom Margrain

School of Optometry and Vision Science, Cardiff University, UK

Purpose
To evaluate the modelling of a focal rod ERG intensity response series with the Naka-Rushton function. The principle was initially assessed using highly averaged data, then a clinical protocol was assessed, with reduced averaging, on a group of normal elderly volunteers. Measurements were taken on two occasions to assess the coefficient of repeatability (CoR).

Methods
Subjects were dark adapted for 25 minutes, after pupillary dilation. DTL fibre was used for both active and contralateral reference electrodes. The stimulus consisted of an array of LEDs (λ 955;max = 454 nm, half-height bandwidth =67 nm), presented at 0.5 Hz, subtending 20° at the eye. A desensitising green ganzfeld surround was used (λ 955;max= 525 nm, half-height bandwidth = 37 nm, 1.67 log Scot Td.s) to suppress the rods of the peripheral retina. For stimuli above the cone detection threshold a constant rod suppressing green background (1500 Scot Td.s) was used to isolate the cone contribution, which was then subtracted from the focal rod ERG. ERGs were recorded in response to 6 intensities (1, 4, 20, 100, 500 and 1000 Scot Td.s), in order of increasing luminance. Two subjects (age 22 and 24) were tested on a single occasion, with 150 averages at the 3 dimmest intensities, and 100 averages at the 3 brightest intensities. 14 further subjects (aged 55 to 71) were recruited and tested on two occasions, 30 to 50 averages were recorded at each intensity.
Responses were fourier analysed to remove noise above 45 Hz, and b-wave amplitude was measured and modelled using the Naka-Rushton function with a least squares paradigm. An alternative approach evaluated the amplitude ratio of the 500 to 20 Scot Td.s responses.

Results
The Naka-Rushton model provided a good fit to the two highly averaged data sets, producing values of 0.88, 1.08 (Log Vmax) and 0.92, 0.90 (Log k). Amplitude ratios of 1.52 and 1.32 were obtained. The elderly subjects, assessed on two occasions, produced acceptable model fits in 21 of 28 tests. Group averaged values for the Naka-Rushton parameters from the successfully modelled data were 1.06 SD 0.19 (Log Vmax) and 1.32 SD 0.32 (Log k); the intersession CoRs for Log Vmax and Log k were 0.26 and 0.28 respectively. The mean ratio for the elderly data was 1.74 SD 0.58, with a CoR of 0.92.

Conclusions
The Naka-Rushton model provided a good fit to the intensity-response data. However the model applied to data collected from elderly subjects, with reduced averaging, was less able to describe the data due to a decreased signal to noise ratio (SNR). For clinical assessment a ratio of two focal rod ERGs at light intensities that approximately correspond to Log Vmax and Log K was more practical. This approach will allow increased averaging within a clinical timeframe, improving the SNR, whilst still providing information regarding the intensity-response relationship.

14:15 – 14:30

L- and M-cone isolating ERGs using silent substitution: comparison of CRT and LED devices

Neil Parry[1], Jan Kremers[2], Ian Murray[3], Declan McKeefry[3] and Naveen Challa[4]

(1) Vision Science Centre, Manchester Royal Eye Hospital
(2) University Eye Clinic, Erlangen, Germany
(3) Faculty of Life Sciences, University of Manchester
(4) Dept of Optometry, University of Bradford

On a device which creates metameric colours using a combination of spectrally tuned sources, it is possible to create stimuli which modulate between two different chromaticities in such a way that the change is only visible to a single cone class. Here we describe the use of these so-called silent substitution stimuli to isolate the ERG responses from long- and medium-wavelength cone photoreceptors in the normal human eye.

Using a 3-phosphor CRT device, driven by a VSG 2/5 card, we constructed stimuli which swept through a range of retinal eccentricities, demonstrating at 30Hz a close correlation with the predicted stimulated cone count. L-cone ERGs are generally higher amplitude than M-cone response and this reflects the L:M cone ratio. We show that L:M ratio is not constant across the retina. In contradistinction, the use of slower rates (12Hz) produces an L:M ERG ratio of approximately unity, which does not vary with eccentricity. This appears to reflect the operation of cone-opponent mechanisms, suggesting that the ERG is able to signal post-receptoral processing.

We have extrapolated the technique to a 4-LED ganzfeld device (Diagnosys ColorDome) which has the advantages of obtaining higher cone contrasts and much higher luminances than the CRT, although the range of spatially-varying stimuli is more limited. The extra LED allows triple silent substitution and gives greater control over rod and S-cone contrast. We have recorded using retinal illuminances of up to approximately 6000 trolands. The data suggest that, at the highest luminances, the L-cone response becomes less linear.

These studies show that, with standard stimulating equipment it is possible to design sophisticated paradigms which give exquisite control over individual receptoral and post-receptoral mechanisms.

14:30 – 14:45

Do measured ERG stimulus parameters determine the response, or are there other factors at work?

M.C. Brown*, R.F. Lowson, R.P. Hagan, A. Small, A.C. Fisher

Medical Physics and Clinical Engineering Dept. & Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool
**email: EDT@MalcolmBrown.com*

Purpose
To test whether full field electroretinogram (ERG) results are the same when using a hand held single eye Ganzfeld stimulator as when using a large bowl 'full face' stimulator.

Method
Full field ERG tests were conducted on 10 volunteers in light and dark adapted conditions, first with a large bowl Ganzfeld stimulator, and then with a single eye hand held unit. The stimulators used were proprietary (Roland Consult, Brandenberg, Germany), and the performance parameters were measured and found to be similar in terms of flash and background luminance and for duration of the flash (both used LED flash generators).

Results
Implicit times were similar for the two stimulators. Response amplitudes were significantly smaller with the hand held unit ranging from 50 – 80% of the responses in the large bowl. The difference was greatest for the dark adapted A wave ($p<0.001$) and light adapted B-wave ($p<0.005$).

Conclusions
Large and small bowl Ganzfeld stimulators for full field ERG may not produce comparable results, even if their measured technical parameters are the same. In this study the small (single eye) unit produced only 50-80% of the amplitude response of the large bowl stimulator, and this ratio was different according to the pathways being tested. The most likely explanation is in the geometry of the units and placement with respect to the eye, achieving a full field stimulus only with the large bowl where the face is placed right within the bowl. This may have important implications for any comparison of results using different stimulators.

14:45 – 15:00

Explicit Detection of PERG above Noise Floor allows for Early Stopping of Recording

L.C. Milner[1], A.C. Fisher[1], M.J. Austin[1], A. Small[1], R.P. Hagan[1], M.C. Brown[1], S.P. Harding[1], D.Simpson[2]

(1) Department of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool
(2) UK Institute of Sound & Vibration Research, University of Southampton, UK*

Aim

Using our previously reported technique of bootstrap resampling (ISCEV 2009) to obtain p-values relating to the presence of a PERG signal we propose to indicate during the PERG recording at what point the protocol can end according to a desired level of confidence (á=0.05) in the presence of a signal, reducing both clinic time and patient discomfort.

Method

The bootstrap resampling method for PERG analysis tests the null hypothesis that no signal exists by comparing a parameter measured during a time-locked response period to a distribution of the same parameter built up by randomly sampling (with replacement) the entire recording. This gives a one-sided p-value to either accept or reject the null hypothesis as a binomial proportion, that is, the amount of times k that the time-locked parameter is smaller than the randomly sampled parameter in n trials. As such, confidence intervals around the p-value can be constructed and we have suggested that as soon as the upper-estimate of the p-value is below the á-significance level then the PERG recording can be stopped.

Results

The upper p-value estimates as calculated in PERG recordings from 18 volunteer eyes indicated that our early stopping criteria had been met after a range of recording lengths, linked to the individual SNR values from each patient's recording. This allowed stopping in some cases after less than 40 epochs, while in other cases the full 80 epochs as prescribed in our local protocol were needed.

Conclusion

Early stopping can be achieved through objective signal analysis and this can save time in the clinic and allow for a more pleasant patient experience. The method is currently not fast enough to run "on the fly" but as yet no particular attention has been given to the speed of our code and we believe that this is easily achievable.

It is suggested that this technique be applied prior to cursoring. Its role in automatic 'objective' reporting of records is presented elsewhere in this meeting (Fisher, Austin et al).

A real time demonstration will be given on synthetic data with realistic auto-regressive noise and clinical data sets.

15:00 – 15:15

Setting Confidence Limits to Automatically-Generated Cursor Positions: A Simple Statistical Approach

A.C.Fisher[1], M.J.Austin[1], L.Milner[1], M.C.Brown[1], R.P.Hagan[1], S.P.Harding[1], D.Simpson[2]

(1) Department of Medical Physics & Clinical Engineering and Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool, UK
(2) Institute of Sound & Vibration Research, University of Southampton*

Purpose

A number of techniques has been proposed recently which identifies automatically cardinal positions (cursor positions) in visual electrodiagnostic recordings. Conventionally, simple time-based coherent averaging is used to recover evoked potential signals: this does not allow for estimation of statistical confidence in the averaged signal, leaving reporting with an unknown uncertainty. Here, using the PERG as an example, a bootstrapping technique is described which can be used to calculate 2D confidence intervals on the locations of the cardinal points of the record, i.e. the positions of N35, P50 and N95. This technique is best applied after the effective SNR of the raw signal is estimated, again using a bootstrap technique: this is described elsewhere in this meeting by Milner, Fisher et al.

Methods

ISCEV standard PERG recordings were collected from 36 normal eyes using a Roland Retiscan system. Confidence intervals on the latency and amplitude of the cardinal points were then derived by repeatedly cursoring bootstrap resampled subsets of the recorded data using an automatic adaptive polynomial fitting method, as available in the Liverpool EYE-EDT-ToolBox.

Results

In our normal group of patients, the mean latency and 95% confidence intervals were 28.8 ± 0.4ms (N35), 51.1 ± 0.3ms (P50) and 97.9 ± 0.6ms (N95) and in terms of amplitude were -0.77 ± 0.1µV (N35), 4.3 ± 0.1µV (P50) and -2.7 ± 0.1µV (N95).

Conclusions

Automatic cursoring of recovered PERGs is straight-forward, accurate, objective and, with the bootstrapping technique, allows for a level of confidence to be expressed explicitly when reporting results. For the first time, this method allows for a measure of the inter-epoch variation in the recorded PERG.

This presentation will be illustrated on clinical data in a real time demonstration run over the Internet using MatSOAP technology. All routines are freely available at www.liverpooleye.org in the Liverpool EYE-EDT-ToolBox of MatLab programs.

15:15 – 15:30

Poster Parade

(The landing outside Hallam View Restaurant)

Moderator: Jamie Healey

Abstracts in alphabetical order

Luminance-response functions for ERG flicker stimulation: Effect of pupil dilatation

Abdlsaed Al Abdlseaed[1], Ruth Hamilton[2], Daphne L McCulloch[1]

(1) Vision Sciences, Glasgow Caledonian University, Glasgow Scotland, UK, G4 OBA
(2) Glasgow University, Glasgow, Scotland, UK, G12 8QQ

Purpose
ERGs are dependant on retinal luminance, which is affected the pupil size. However, constriction of natural pupils is much greater for flickering stimuli than for steady backgrounds. We characterise the differences between ERG amplitudes for stroboscopic flicker at the flicker frequency (F1) and at the first harmonic (F2) for natural and dilated pupils.

Methods
Participants were 11 healthy adult volunteers with no visual or ocular motor dysfunction and corrected visual acuity of 6/6 (0.0 Log MAR) or better in each eye. ERGs were recorded monocularly (using a light excluding patch) with natural and with dilated pupils to flicker at 12.66Hz. The stimuli were 4 ms pulses produced by LEDs in ganzfield (Espion Colordome) on a background of 21.3 cd/m^2. Flicker data was re-sampled and the magnitudes of Fourier components at F1 and at F2 (25.3 Hz) were measured. Luminance-response (L-R) functions were fit using a logistic growth curve or a 'photopic hill' model incorporating a Gaussian and logistic curves[1].

Result
For F1, 8/11 subjects demonstrated a photopic hill-shaped L-R function with natural pupils and 9/11 with dilated pupils. For F2 L-R functions were fit with a simple logistic growth function.
For F1 we compared L-R functions parameters for natural and dilated pupils between subjects with the same shape of L-R function (eight photopic hills and two simple logistic growth functions). L-R functions were similar but there was a trend for the Gaussian 'hill' component to be higher with dilated pupils (p=0.09, paired t-test). For F2 the saturated amplitude of the logistic growth function (Vb max) was smaller with natural pupils (p=0.02, paired t-tests). In addition, the amplitude parameters showed lower variability with the natural pupil than with the dilated pupil.

Conclusions
Flicker ERGs with dilated pupils have larger responses at the first harmonic of the flicker frequency (F2) and show a trend towards an increase in the photopic hill component for the ERG magnitude at the flicker frequency.

1 Hamilton R, Bees MA, Chaplin CA, McCulloch DL (2007). The luminance-response function of the human photopic electroretinogram: A mathematical model. Vision Research 47(23):2968-2972

PERIODIC SIGNALS: WHEN DOES THE DATA NEED TO BE RESAMPLED TO CORRECT FOR NON-INTEGER STIMULUS CYCLES?

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Purpose

Periodic waveforms such as the 30 Hz flicker ERG are best analysed in the frequency domain. A constraint of such frequency domain analysis is the need for an integer number of stimulus cycles per data epoch. Sampling frequency may be fixed at 1 kHz, so a 30 Hz flicker ERG with a (commonly-used) 1024 ms epoch would contain 30.72 stimulus cycles – a non-integer. Stimulus periods may be limited to millisecond resolution, again creating a non-integer number of stimulus cycles. Data can be truncated to the nearest complete cycle and re-sampled to retain 1024 data points but this has an additional computational overhead. The purpose of this study was to determine the relationship between non-integer stimulus cycles in the data epoch and the signal-to-noise-ratio (SNR) at the stimulus frequency.

Methods

Three flicker ERGs were recorded from six normal adults using an Espion system. The data epoch was 1024 ms and the sampling frequency was 1 kHz (1024 data points per epoch). Averaging (N=6) was used. A stimulus frequency of 30.0000 Hz (30.72 cycles per epoch) was requested: the Espion in fact delivers this at 30.3030 Hz (31.0303 cycles per epoch). Test A: raw data was analysed in the frequency domain (FFT, Microsoft Excel) and SNR was calculated (amplitude at bin containing 30.3030 Hz divided by mean amplitude of neighbouring bins). Test B: raw data was truncated to 31 cycles (1023 ms), re-sampled to retain 1024 data points, and analysed as above. Test C: To emulate electrophysiological data acquired with a stimulus frequency of 30.0000 Hz, the raw data was fractionally stretched to create a 1024 ms epoch with 30.7200 stimulus cycles, then analysed as above. SNRs were tested for differences using a paired t-test with á=0.05 between tests A and B and between B and C. For theoretical comparison, three noise-free, 1024-data-point 'flicker ERGs' were synthesised by sinusoids: A, 30.3030 Hz with a 1024 ms data epoch (31.0303 cycles); B, 30.3030 Hz with a 1023 ms data epoch (31.0000 cycles) and C, 30.0000 Hz with a 1024 ms data epoch (30.7200 cycles).
Results: For test A, SNR values were 17.3–35.4; for test B, 15–44 and for test C, 2.8–3.4. SNRs increased between test A (raw) and B (re-sampled), but was not significant (p=0.614). However, SNRs from the 30 Hz 'raw' data in test C were significantly lower than B (re-sampled) (p=0.003). For the synthesised data, SNRs for ERG A was 33, for ERG B was >1000 and for ERG C was 3.3.

Conclusions

Providing the true stimulus frequency is known, a small decimal part of 0.0303 non-integer number of cycles in the data epoch has only a small effect on the SNR, and physiological noise rather than spectral leakage will mask the signal. However, the larger decimal part of 0.7200 non-integer number of cycles has a significantly detrimental effect. Acceptable decimal portions of non-integer numbers of cycles can be predetermined according to the SNR threshold used.

Acknowledgement: This paper was presented at the 47th Annual Symposium of the International Society for Clinical Electrophysiology of Vision, in Padova, Italy, 6 to 10 July 2009.

AN EXAMINATION OF PERG, ERG & mfERG AMPLITUDE RESPONSES FROM DTL©-LIKE ELECTRODES WITH DIFFERING FIBRES: A SIMPLE SCALING MODEL IS PROPOSED

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Introduction

The silver-thread corneal (scleral) electrode (after Dawson, Trick and Litzkow) is marketed as the DTL© and the DTL-Plus© by Diagnosys LLC. Both use multi-filament silver-coated nylon: the former is 7-stranded and the latter 9-stranded. A study by Wright et al (ISCEV, 2008) employed the method of Vaegan to compare the peak-to-peak (p-p) amplitude response in the ERG and mfERG using the Eye-EDT-ToolBox (www.liverpooleye.com) objective reporting algorithm (see elsewhere in these proceedings Fisher et al *). They found that the 7-strand DTL gave p-p amplitude responses ~1.15 greater ($p = 0.048$) than the 9-strand DTL-Plus. However, the signal-to-noise ratio (SNR), inferred from variation in the p-p, was less in the DTL-Plus ($p < 0.05$). The physical basis of these findings was unexplained.

Purpose

To repeat the original study of Wright and extend the reporting to ERG a and b waves (scotopic and photopic), mfERG NI and P1 components, and the PERG N35, P50 and N90 cardinal points (amplitudes). Additionally, a third electrode manufactured exactly to the DTL-Plus method but using 7-stranded fibre from Unimed Ltd. (purportedly as used in the 'standard' Diagnosys DTL) was included.

Method

Fourteen visually-healthy subjects were recruited and recordings made on a Retiport© instrument (Roland Consult, Brandenburg) as per the ISCEV Standards (ERG and PERG) and ISCEV Recommendations (mfERG), and interpreted using the Eye-EDT-ToolBox. In all 14 subjects, the ERG and mfERG amplitudes were measured for the DTL and DTL-Plus randomly assigned to left and rights eyes. Similarly, in a subset of 8 subjects, PERG amplitudes and SNR (see *) were recorded for the DTL-Plus and DTL-Plus-Unimed-fibre electrodes. A transfer (amplitude gain) function (after Vaegan) is reported as the aggregate slope of the regression lines for DTL vs. DTL-Plus and vice versa.

Results:

Comparisons were made on the basis of the twin-tailed paired t-test across left and right eyes in each subject: H0 is no difference at $p = 0.05$.

1. DTL versus DTL-Plus (7-stand vs. 9-strand):
a. ERG scotopic a & b waves AND photopic a wave, H0 rejected (different?)
b. ERG photopic b wave, H0 not rejected (the same?)
c. mfERG N1 & P1, H0 not rejected (the same?)
2. DTL-plus versus DTL-Plus-Unimed-fibre (7-stand vs. 9-strand):
a. PERG signal-to-noise (SNR), H0 not rejected (the same?)
b. PERG N35, P50 & N90, H0 not rejected (the same?)
3. Transfer functions (DTL wrt DTL-Plus), for all ERG, mfERG & PERG
a. where H0 is rejected, in range [1.10 … 1.125]
b. where H0 is not rejected, in range [0.8 … 1.05]
4. Transfer functions (DTL-Plus wrt DTL-Plus-Unimed-fibre), for PERG

H0 not rejected, in range [0.94 … 1.1]

Conclusion

The simple linear scaling of amplitude sensitivity ** as reported previously of DTL wrt DTL-Plus holds for ERG scotopic a & b wave and for photopic a wave. It does not hold for ERG photopic b wave, mfERG N1 & P1 and PERG SNR & N35, P50 & N90. The apparent difference ** is not explained simply by 7-strand (Unimed fibre) as opposed to 9-strand construction.

A COMPARISON OF THE PARAMETERS OF OBJECTIVE AND SUBJECTIVE MEASURES OF DARK ADAPTATION *

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Purpose

Current methods of monitoring dark adaptation are primarily based around subjective psychophysical procedures. A comparison of the parameters of photostress recovery using psychophysical and electrophysiological techniques will demonstrate the viability of objective methods as an alternative measure of dark adaptation.

Method

Photostress recovery after a 99% bleach of rod and cone photopigment was monitored in two normal subjects (AB and AG) using two electrophysiological and one psychophysical method. All electrophysiological stimuli were generated by a light emitting diode (LED) miniature ganzfeld stimulator held at the eye. Signals were amplified, bandpass filtered (1-100Hz) and averaged using a Medelec Synergy EP system.

Full field cone flicker electroretinograms (ERGs) were recorded in response to an amber (¥ëmax = 595nm, half-height bandwidth = 17nm) square wave flickering (41Hz) stimulus, with a time-averaged illuminance of 1500phot.td. Four pre-bleach ERGs were recorded as a baseline measure. Post-bleach ERGs were recorded every 20 secs for 5 mins, with 100 responses averaged on each trace. The amplitude of the first harmonic was plotted as a function of time after the bleach.

Full field rod ERGs were recorded in response to a blue (¥ëmax = 454nm, half-height bandwidth = 67nm) 5scot.td.s flash, duration 5ms and temporal frequency of 0.5Hz. Post-bleach ERGs were recorded at 2 minute intervals for 35 mins. 30 responses were averaged on each trace and b-wave amplitude was plotted as a function of time after the bleach, after removal of high frequency noise (>45Hz) by fourier analysis.

Finally, the Goldmann-Weekers adaptometer was used to measure dark adaptation psychophysically using a method of ascending limits. The stimulus subtended 6.6¡Æ at the eye and was located at 11.8¡Æ in the inferior field.

All recovery data was fitted, using a least squares paradigm, with an exponential model and the time to half recovery assessed.

Results

The exponential model provided a good fit to the rod and cone ERG and psychophysical recovery data. The times to half recovery (given for subjects AB and AG) for photopic ERG amplitudes were 1.22 and 0.96 mins, and for scotopic ERG amplitudes were 14.85 and 10.3 mins. For the Goldmann-Weekers adaptometer, times to half recovery for the cone branch were 1.46 and 1.12 mins, and for the rod branch were 14.45 and 13.1 mins.

Conclusion

The ERG can be used as a simple objective measure of rod and cone dark adaptation. The exponential model provided a good fit to all recovery data. The times to half recovery were comparable to those obtained using a psychophysical technique. This indicates that the ERG provides a potential clinical means of assessing dark adaptation, which avoids the problems inherent in subjective psychophysical strategies.

INVESTIGATING THE TOPOGRAPHY OF ERG LATENCY ACROSS THE RETINA

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(2) Clinical Eye Research Centre, Royal Liverpool University Hospital, Liverpool, UK.

Purpose
It has been well documented that the density of the response changes across the retina as demonstrated by the mfERG. This study investigates if the latency of response changes from the centre of the macula to 21 degrees peripheral. Latency was examined at fast rates (m-sequence run at 60Hz) at slow rates (m-sequences ran at 60Hz with 4 blank filler frames).

Method
Two hexagons were run with the same m-sequence offset by 52 steps in the m-sequence. The central hexagon covered 8 degrees diameter and the peripheral hexagon situated 16 degrees nasally (centre to centre) was also eight degrees in diameter. Responses were collected from the RE only (n=18) and the pupil was dilated with 1% Tropicamide. Local regional ethical committee approval was granted and informed consent from the subjects was collected. Testing adhered to the declaration of Helesinki.

Results
Latency was statistical slower centrally than the periphery at both rates.

Conclusion
The latency of the mfERG is different centrally than peripherally and this latency shift is more obvious at slow rates.

FULL-FIELD ERG VARIABILITY IN PATIENTS WITH FUNDUS ALBIPUNCTATUS (FA)

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(2) Institute of Ophthalmology, London, UK

Purpose
To compare the range of full-field ERG abnormalities in patients with fundus albipunctatus (FA).

Methods
A cohort of patients with fundus albipunctatus was assessed by clinical examination, electrophysiology and autofluorescence imaging. Electrophysiology was performed to incorporate the relevant ISCEV Standards; significant additions included the use of red stimulation under dark adaptation and the use of prolonged dark adaptation (DA), usually one eye overnight. Most patients gave permission for DNA screening which confirmed RDH5 mutation.

Results
Patients with FA showed a variable degree of generalized cone system dysfunction, with only some patients showing full-field photopic ERG abnormalities. After a standard 20-minute period of DA, rod specific ERGs varied between undetectable and subnormal; red flash ERGs were dominated by the cone component and bright flash ERGs were usually electronegative, in keeping with dark-adapted cone system function. Prolonged DA resulted in scotopic ERG normalization in all but one genetically-confirmed case.

Conclusion
The severity of ERG abnormality varies in patients with fundus albipunctatus. Standard rod ERGs vary in amplitude suggesting the availability of chromophore may differ in patients with different mutations. Scotopic ERGs are dominated by cone system activity, exposed in the absence of normal rod function, and normalize after prolonged DA in most but not all cases.

SERIAL IMAGING AND FUNCTIONAL AND STRUCTURAL CORRELATES OF HIGH DENSITY RINGS OF FUNDUS AUTOFLUORESCENCE IN RETINITIS PIGMENTOSA

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

Methods
Ninety patients with a clinical diagnosis of RP confirmed by ERG were examined, including 26 with Usher syndrome. All had a visual acuity of 6/9 or better and an abnormal ring of high density fundus AF. Repeat AF imaging was performed in 25 cases after periods of up to 7 years. All had international-standard pattern ERGs (PERGs). Fine matrix mapping (FMM) was performed in 12 cases to test sensitivity at 100 macular locations at 1° intervals. Ocular coherence tomography (OCT) was performed in 12 others.

Results
Serial AF revealed progressive ring constriction in 14 of 25 cases. Ring radius reduction ranged up to 40% at rates of 1.5-16% per year. Fifty one of 90 subjects had pattern ERG evidence of macular dysfunction. The AF ring radius correlated positively with PERG P50 ($R=0.75$, $p<0.005$, $N=87$). FMM showed that the ring encircled areas of preserved photopic sensitivity and was concordant with a steep gradient of sensitivity loss (N=12 subjects). Scotopic sensitivity losses encroached upon the central macula (N=10). There was high correlation between AF ring size and the lateral extent of outer retinal layer preservation (slope = 1, $r = 0.93$, $p<0.05$).

Conclusions
High density AF rings show progressive constriction in a high proportion of individuals with RP and preserved visual acuity. The rate of ring constriction varies between patients. The rings correlate with measures of macular function, encircle areas of preserved outer retina and may be of prognostic value in predicting retention of good central vision.

THE PHOTOCURRENT RESPONSE OF DARK-ADAPTED PRIMATE RODS

J.G. Robson and L.J. Frishman

University of Houston College of Optometry

PURPOSE

Although the extracellular current generated by light activation of retinal rods can provide a major contribution to the flash ERG, all except the very earliest part of the rods' response is obscured by signals generated by the slightly delayed activation of more sensitive post-receptoral retinal cells. Given this situation, it is frequently desirable to be able to estimate the contribution of the rod photocurrent to the later part of the ERG by extrapolating that early portion of the ERG that can be attributed to rods alone. This extrapolation requires that a suitable model description of the complete timecourse of the photocurrent response of rods be available. A model of the rod response that is suitable for this purpose can be developed using data obtained from suction-pipette recordings of the outer-segment current of rods in vitro together with ERG recordings of the effect of rod stimulation on the amplitude of responses to high energy probe flashes that saturate the rods in a few milliseconds.

METHODS

We have made 1) measurements of the effect of weak test stimuli on the amplitude of high-energy probe-flash responses delivered at various times after the test flash in dark-adapted anaesthetized macaques using a minimum interval of 2 minutes between successive probe flashes, as well as 2) recordings of the initial limb of the a-wave for a range of stimuli. It is easier to make satisfactory probe flash measurements in anaesthetized macaques than in humans because of the long time between probe flashes that is required to obviate effects of adaptation.

RESULTS

Based on photocurrent recordings from human rods in vitro (Kraft et al., 1993) together with our ERG recordings from macaque, we have modified the model of Robson et al. (2003) to provide a better description of the later part of the rod response. In this new model it is assumed that the activation of rhodopsin molecules lasts for a fixed time rather than for exponentially distributed times as had previously been assumed. We have also used a new formulation of the saturating non-linearity that is assumed to operate at each instant on the output, R, of the linear transduction cascade to give rise to the recorded voltage, V. This function, $V = Vmax \{1 \exp(-Rn/kn)\}1/n$, is a form of the exponential saturation function seen in single rods that has been modified to allow for the heterogeneity of rod sensitivity in vivo by adding the exponent n.

CONCLUSION

We have provided a model of the photocurrent responses of dark-adapted rods that takes known physiology into account and that enables the contribution to the ERG of the rod photocurrent to be calculated based on ERG measurements made at early times after the flash.

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INVESTIGATING THE REPEATABILITY OF THE PATTERN REVERSAL VISUAL EVOKED POTENTIAL IN A SUBJECT OVER A PERIOD OF MONTHS

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Introduction

Often, to assess the progression of a condition such as raised intra-cranial pressure, or to monitor the effects of a drug such as Ethambutol, the PRVEP of a patient is monitored over a long timeframe. If the amplitude of the responses decreases significantly compared to the baseline then an intervention is usually undertaken. However, it is not known how stable the amplitude of the PRVEP is to repeated measurements, and it is possible that a natural variation of amplitude occurs.

Method

Two subjects were chosen and their PRVEPs were measured at various intervals over an eight month period from December 2008. The minimum period between measurements was one week and the maximum was 2 months. Measurements followed a standard protocol, where the same person recorded the VEP, room lights were on, subject was 1m from screen and approximately 64 reversals made up each average. Standard check sizes of 60', 30', 15' and 7.5' were recorded monocularly.

The amplitudes and latencies of the P100 were analysed to provide a mean and standard deviation for both subjects, as well as the upper and lower confidence intervals.

Results

These initial results show that the latency of the P100 is stable over repeated testing with a standard deviation in the order of 3% of the mean value for each subject, with the maximum standard deviation of the latency being 6% on the smallest check size.

The amplitude of the P100 however is quite variable, with a standard deviation ranging between 7% of the mean value at the larger checks, to 40% of the mean value at the smaller checks.

Conclusion

Early results suggest the natural variability in P100 amplitudes is large, and can even be 100% between the upper and lower limit. This variability may suggest that the PRVEP is not an appropriate tool for monitoring raised intra-cranial pressure or drug toxicity. This will be further investigated in a more detailed study using normals and cranio-facial patients.

REPEATABILITY AND EFFECT OF REFRACTIVE ERROR CORRECTION ON MULTIFOCAL ERG IN PATIENTS WITH QUERY RETINAL DYSFUNCTION

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Purpose
To investigate repeatability of the mfERG and evaluate the influence of refractive error correction on the mfERG in patients with query retinal dysfunction.

Method
The mfERG was recorded for 64 patients with query retinal dysfunction using the VERISTM system (Version4). Hexagon pattern stimulus with 61 elements, covering central 60º of the visual field was used. Patients were divided into two groups (A & B), based on requirement of refractive correction for near acuity (VA) using the Lighthouse near vision chart. The mfERG was recorded twice consecutively for group A patients who didn't need refractive correction. The mfERG was recorded one run with and one run without refractive correction for patients in group B. The lenses varied from -6.5 D to +8 D and were placed in a trial frame. The viewing distance was adjusted. The response sampling rate was 16 Hz giving a sampling interval of 0.83 ms. The net recording time for each run was about 8 minutes. Patient pupils were dilated with 1% Tropicamide and the average pupil size was 7 mm for patients in both groups.

The first kernel responses were grouped into 4 concentric rings and the P1 and N1 amplitudes, and P1 latency of response were analysed. Coefficient of variation (CV) and intraclass correlation coefficient (ICC) were calculated and evaluated by Wilcoxon test and Mann Whitney test.

Results
There was no significant difference in amplitudes and implicit times between the two recordings in patients of group A. In group B patients the differences between the two recordings were not significant in most measurements. The variability of the peak amplitude was much higher than latency in all eccentricities.

Conclusions
This study showed good repeatability of mfERG in patients with or without retinal dysfunction. The CV values decreased with eccentricity and the variability was much higher for response amplitudes than latency.

The mfERG responses were not influenced by refractive blur under the parameters tested in this study. The variability of the mfERG recorded with and without refractive correction was greater in patients with higher refractive errors but did not reach statistical significance.

The most important factor for obtaining a reliable mfERG recording was patients' fixation. Refraction is needed to get good enough VA for fixation. However refraction for OPTIMAL acuity may not be essential, thus resulting in improved clinic efficiency and reduced patient fatigue.

Tuesday 15th September

09:15 - 12:00
Session 2 Science programme Chair TBC

Nitty-Gritty
09:15 - 09:30
Refraction
Jon Whittle
Royal Hallamshire Hospital, Sheffield

09:30 - 09:55
A Guide to Nystagmus
Helen Griffiths
Royal Hallamshire Hospital, Sheffield

09:55 - 10:10
Getting the most from your Ganzfeld
Chris Hogg
Moorfields Eye Hospital, London

10:45 - 11:45

Guest Lecture

Ocular Tumours

Professor I G Rennie

The University of Sheffield

11:45 – 12:00

The timecourse of single-photon signals in the dark-adapted retina

J.G. Robson and L.J. Frishman

University of Houston College of Optometry

PURPOSE

To compare the timecourse of the responses to single photons of primate rods with that of the responses to single photons of rod bipolar cells and to relate these to a) the overall temporal frequency characteristics of dark-adapted vision (as manifest in the psychophysically determined visual modulation sensitivity function) and b) the responses of ganglion cells recorded from baboon retina in vitro (unpublished data kindly provided by Marshak, Glickman and Akimov).

METHODS

The timecourse of the responses to brief flashes of retinal rods in anaesthetised macaques was ascertained from the ERG using the high-energy probe-flash technique in conjunction with recordings of the early part of the a-wave. The timecourse of responses within the range where the amplitude of the response was proportional to stimulus energy was assumed to reflect single-photon activation of rods. The contribution of macaque rod bipolar cells to the ERG (PII) was obtained by recording the ERG after supressing the response of other inner-retinal cells with intravitreally injected ionotropic glutamate blockers. The timecourse of PII in the range in which its amplitude was proportional to stimulus energy was assumed to represent the response to single photons. PII was analyzed into a fast component that reflects the post-synaptic current and represents the signal that is transmitted by the post-receptoral cells and a slow component that is generated as a result of the release of K+ into the extracellular space of the retina. The sensitivity to sinusoidally modulated light of an ensemble of retinal rods or post-receptoral cells operating at a mean luminance low enough for the stochastic single-photon signals to be essentially separate in time (< ~0.1 scotopic Td in human, i.e. < ~1 R* s-1/rod and < ~20 R* s-1/rod bipolar cell) was obtained by Fourier transformation of the single-photon responses.

RESULTS

The single-photon response of dark-adapted rods rises earlier but declines later than the response of rod bipolar cells. The integration time of the rod response (~300ms) was found to be roughly 3 times greater than that of rod bipolar cells (~100ms). The attenuation of high frequencies in the signal from an ensemble of rods started at a frequency (~1Hz) that is substantially lower than the frequency (3 – 4 Hz) above which the signal carried by the activity of an ensemble of rod bipolar cells becomes attenuated. The temporal contrast threshold in human vision for sinusoidal modulation of very weak light has been found (Kelly, 1961) to start rising at frequencies above about 7Hz, the same frequency as that at which the response of baboon retinal ganglion cells starts to fall.

CONCLUSION

The temporal characteristic of human vision at very low light levels reflects the timecourse of the single-photon responses of retinal ganglion cells whose duration is about one half that of the responses of rod-bipolar cells. The duration of the single-photon responses of rod bipolar cells is 1/3 to 1/4 that of the responses of rods themselves.

13:00 – 13:15

ERG findings in patients with a K+ channelopathy due to a mutation in KCJN10 gene *(Presented at ISCEV 2009)*

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(3) Physiology, University of Regensburg, Regensburg, Germany

PURPOSE
KCNJ10 has demonstrated importance in retinal function in animal experiments. Recently, mutations in KCNJ10 were recognised as pathogenic in man, causing a constellation of symptoms, including epilepsy, ataxia, sensorineural deafness and a renal tubulopathy designated as EAST syndrome. Here we study the impact of KCJN10 mutations on the human ERG.

METHODS
Corneal ganzfeld flash ERGs were elicited in response to scotopic, (scot 0.001 – scot 10), and photopic, (phot 0.3 -10), stimuli in 2 unrelated patients. Each patient has EAST syndrome with an underlying homozygous missense mutation c.194C>G;p.R65P of the KCJN10 potassium channel gene. Each patient underwent an ophthalmological examination.

RESULTS
Each patient had normal visual acuity and fundal appearance. Scotopic ERGs to flash intensities scot 0.01 to scot 0.1 $cd \cdot s \cdot m^{-2}$ showed a delay before the onset of the b-wave compared to controls. B-wave amplitudes to the dimmer stimuli were small, but amplitudes then increased sharply with flash intensity. Naka Rushton functions were fitted to the first limb of the V/I curve. Log K, an index of retinal sensitivity derived from these functions for the patients were 0.006 & 0.009 respectively, reduced more than 3SD from the mean LogK of 14 controls 0.002, SD 0.00078. Photopic ERGs also showed a delay in the time to peak of b-wave and the amplitude of the photopic negative response was reduced 3SD compared to controls.

CONCLUSION
Changes in the timing and shape of the human ERG occur in the presence of a KCJN10 mutation and show a role of this potassium channel in the retina modifying intra-retinal currents.

13:15 - 13:30

Phenotypic assessment of autosomal recessive Congenital Stationary Night Blindness with and without mutations in GRM6

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PURPOSE
To describe cases of autosomal recessive congenital stationary night blindness (CSNB) with and without mutations in GRM6.

METHODS
Eight patients from 6 pedigrees were ascertained with night blindness including a sibship and a mother and infant daughter from a consanguineous pedigree. The adult cases (N=6) and one 5-year-old child underwent full-field and pattern electroretinography (ERG) incorporating the International-standard protocols. Additional ON-OFF ERGs (stimulus duration 200ms) and short-wavelength flash ERGs were performed. The 15-month-old infant was tested using skin electrodes attached to each lower eyelid according to a shortened protocol that included photopic 30Hz flicker and scotopic ERG testing. Fundus photographs and fundus autofluorescence were reviewed. The coding region and intron-exon boundaries of GRM6 were sequenced.

RESULTS
Seven of 8 individuals had mild to severe myopia. In all patients that underwent International-standard testing, the rod ERG was undetectable and the bright flash ERG (flash intensity 11.5 cd.s.m-2) was markedly electronegative. In all but two cases, photopic 30Hz flicker ERGs were borderline in terms of timing or marginally delayed; normal in terms of amplitude. The transient cone ERG had a broad bifid a-wave and sharply rising b-wave without oscillatory potentials. The ON-OFF ERGs showed severe ON b-wave reduction and sparing of the OFF response. In an elderly brother and sister with myopic degeneration there was additional delay in the 30Hz flicker ERGs and the brother had additional scotopic bright flash ERG a-wave reduction. The surface flash ERGs in the infant were qualitatively identical to those recorded in her mother, in keeping with pseudo-dominant inheritance. The pattern ERG was preserved in one case. DNA sequencing revealed mutations in GRM6 in 4 of 8 cases.

CONCLUSIONS
A form of autosomal recessive complete CSNB is described consequent upon mutation in GRM6. Autosomal recessive complete CSNB is a heterogeneous condition.

13:30 – 13:45

Optimisation of Signal Quality During Multimodal Imaging using Combined OCT/SLO and Micro-Multifocal ERG

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Purpose
To determine the optimal micro-multifocal electroretinogram (micro-mfERG) recording parameters for use during multimodal imaging (MMI) using combined scanning laser ophthalmoscope (SLO), optical coherence tomography (OCT) and micro-mfERG.

Methods
An OCT/SLO scanner (OTI; Toronto, Canada) with an integrated organic light emitting diode (OLED) display was used to provide simultaneous micro-mfERG recording (SHIL; Glasgow, UK), SLO and OCT imaging of up to the central 24 degrees (multimodal imaging; MMI).

A series of MMI recordings with differing micro-mfERG recording parameters was performed on 10 healthy control subjects. The effect of stimulus intensity on micro-mfERG signal quality was assessed by performing MMI at three OLED luminance settings. The influence of spatial stimulus resolution was investigated by performing MMI with micro-mfERG stimulus paradigms composed of 7, 19 or 37 hexagonal elements. A black filler frame was inserted into the stimulus m-sequence to ascertain the effect of temporal resolution on micro-mfERG signal quality. The influence of stimulus driving frequency on micro-mfERG signals was assessed by conducting tests at stimulus presentation rates of 60 Hz and 75 Hz.

Results
Micro-mfERG recordings were analysed in relation to response amplitudes and implicit times and also according to signal quality. Signal quality was assessed by determining mean signal to noise ratio (SNR) of waveforms derived from each recording. Based on our experience with conventional mfERG recordings, the target micro-mfERG signal quality was 25dB or higher. Without post processing or spatial averaging of the signals, a 19 element stimulus paradigm was the highest spatial resolution that provided micro-mfERG responses within the SNR target. Recordings performed at medium OLED luminance had better signal quality than those conducted at low or maximum luminance. SNR was not improved by slowing the stimulus using a black filler frame. Recordings performed at a stimulus frequency of 75 Hz had significantly better signal quality than those conducted at 60 Hz.

Conclusions
Optimal micro-mfERG signal quality during multimodal imaging was achieved using a 19 element stimulus with sub-maximal OLED luminance, no filler frames and a driving frequency of 75 Hz. These micro-mfERG parameters are now being used in clinical MMI recordings and allow the recovery of robust signals for clinical interpretation without requiring post-processing of the recovered data.

13:45 - 14:00

Comparing localised retinal function from mfERG with estimates of cone density from in vivo imaging of the photoreceptor mosaic using a modified Heidelberg Retina Tomograph

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Purpose
To investigate the relationship between multifocal electroretinography (mfERG) responses and measures of cone packing density from in vivo imaging of the retinal photoreceptor layer using a modified commercially-available scanning laser ophthalmoscope.

Methods
A Heidelberg Retina Tomograph, (HRT1) was modified to give 1x1° and 2x2° high resolution images of the retinal photoreceptor mosaic without adaptive optics in two normal subjects. Individual cone cells were identified from retinal images of the parafoveal region out to 4mm eccentricity and used to determine cone density as a function of retinal eccentricity. This was compared to the spatial variation in retinal function, determined in the same subjects from mfERG responses to a high resolution (241-element) stimulus array.

Results
The modified HRT1 device produced reliable images of central cone mosaic structure in each subject. Estimates of cone density ranged from around 19,000 to 5,000 cells/mm² between 0.6mm and 3mm retinal eccentricity. Cone density was strongly linearly correlated (r=0.98) with mfERG amplitude within the central retina.

Conclusions
The variation of cone photoreceptor packing density with retinal eccentricity compared well with published data from histology and adaptive optics imaging. Retinal function determined from mfERG amplitude appears to directly reflect the density of the cone cells. There is a need to more fully explore the potential and clinical utility of the modified HRT to produce retinal cone counts in diseases that affect photoreceptor density and investigate how this relates to changes in local retinal function.

14:00 – 14:15

Ocular pigmentation in light- and dark- adapted ERGs

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Purpose
To investigate the normative ERGs in subjects identified by iris colour, and inferred retinal pigmentation, under both dark- and light-adapted conditions and to discuss possible causes of any differences.

Methods
Two groups of ophthalmologically normal, young volunteers (20-22 years) were studied: seven blue-eyed Caucasians and seven brown-eyed Asian subjects. Fundus photography confirmed a strong correlation between iris colour and fundus pigmentation. After pupil dilation (tropicamide 0.5%) and dark-adaptation (20 min), a luminance-response ERG series was recorded using a Burian Allen contact lens electrode with topical anaesthetic (Oxybuprocaine 0.4%) and lubricant (Celluvisc). The non-test eye was covered by a light-occluding patch. ERGs were recorded using an Espion (Diagnosys UK) system with a ganzfeld ColorDome stimulator. Subjects were then light-adapted for five minutes to a 25 cd/m2 background; a second luminance-response series was recorded background. ERG a- and b-wave amplitudes were plotted versus luminance and curves were fitted to the data with appropriate equations: a logistic growth ("Naka-Rushton") function gives parameters Vmax (μV) and  (sensitivity, cd s m-2) while the photopic hill function has a Gaussian component with height G (μV) and μ (sensitivity, cd s m-2) as well as a logistic growth component. The study was approved by the local Ethics Committee and informed consent was given.

Results
Dark-adapted a-wave amplitudes (logistic growth function) reach a larger Vmax for blue eyes than for brown eyes (403 μV versus 323 μV, p=0.05), but eye colour did not affect a-wave sensitivity (0.92 cd s m-2 versus 0.76 cd s m-2, p=0.4). Dark-adapted b-wave amplitudes (logistic growth function) do not differ in Vmax for blue eyes and brown eyes (528 μV versus 455 μV, p=0.2), nor did eye colour affect b-wave sensitivity (0.005 cd s m-2 versus 0.007 cd s m-2, p=0.6). Light-adapted a-wave amplitudes (logistic growth function) do not differ in Vmax for blue eyes and brown eyes (103 μV versus 96 μV, p=0.14), nor did eye colour affect a-wave sensitivity (2.7 cd s m-2 versus 3.5 cd s m-2, p=0.14). Light-adapted b-waves fitted with the photopic hill function showed a substantially larger Guassian component for blue eyes than for brown eyes (86 μV versus 157 μV, p=0.005), but eye colour does not affect the Gaussian sensitivity (0.69 cd s m-2 versus 0.66 cd s m-2). The logistic growth component of the photopic hill does not differ with eye colour (Vmax, 81 μV versus 78 μV, p=0.9; sensitivity -0.002 cd s m-2 versus 0.006 cd s m-2, p=0.9). Neither a-wave nor b-wave ERG latency was affected by eye colour under dark- or light-adapted conditions.

Conclusion
These results have implications for normative data sets. ERGs from blue eyes reach larger dark-adapted a-wave amplitudes than brown eyes, suggesting greater responsivity of the rod photoreceptor systems. This could be explained by increased light scatter from the paler fundi of the blue-eyed individuals giving greater effective retinal illuminance. Additionally, ERGs from blue eyes have larger b-waves for stimuli in the mid-range of the luminance-response function as shown by the larger Gaussian components for the photopic hill, which may reflect off-responses. Off-responses, with contributions from both hyperpolarising ON bipolar cells (the ON pathway) and from depolarising bipolar cells (the OFF pathway), become later for stronger flashes. Further experiments with prolonged stimuli could identify the mechanisms underlying the non-linear differences based on ocular pigmentation.

14:45 - 15:00

Asymmetries in evoked potentials in children...what do they mean?

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Purpose
To study the importance of half-field testing in explaining full-field VEP asymmetries in children.

Methods
This was a retrospective case review study examining half-field pattern reversal VEP data collected from the Visual Electrophysiology Unit at Great Ormond Street over a 6-month period. Forty-seven patients (age range: 3 years 7 months to 16 years 8 months, mean age: 9 years 9 months) had both monocular full-field and half-field pattern reversal VEPs to test checks subtending 50 minute of arc in a 28 degree test field. Silver-silver chloride electrodes placed at the inion, Oz, O1 and O2 were referred to Fz. Monocular full-field data were visually inspected and categorised according to the degree of transoccipital asymmetry (that is, polarity reversal, greater than 50% difference, less than 50% difference and latency difference). Half-field data were then inspected for the presence of a half-field deficit to explain any full-field asymmetry. Four interesting cases will be presented to highlight the importance of half-field testing and details about an appropriate protocol to use in children will be discussed.

Results
The full-field monocular VEPs were asymmetrical in 87% of patients (40 out of 46). Of these 40 patients, 7 patients had one symmetrically distributed full-field for one eye. The remaining 33 patients had asymmetrically distributed full-field VEPs for both eyes. A polarity reversal between lateral channels were seen in 9% (3 of 33 patients), a greater than 50% difference in amplitude between lateral channels was seen in 18% (6 patients), a less than 50% difference in amplitude between lateral channels was seen in 55% (18 patients) and a latency difference between lateral channels was seen in 18% (6 patients). Half-field data showed that 13% of the patients (6 out of 46) were found to have a typical half-field distribution. Of the remaining 40 patients, 60% (24 patients) showed a half-field deficit of some kind, including bi-temporal, bi-nasal and homonymous half-field deficits. The other 40% (16 out of 40 patients) had atypical half-field distributions which when summated could explain the full-field transoccipital asymmetry.

Conclusions
Half-field pattern reversal VEPs are needed to explain full-field asymmetries in children and should be done wherever possible in co-operative children in a 28 degree test field. 60% of patients with full-field asymmetry reflect a pathway deficit.

15:00 – 15:15

Relationship between VEP Trans-Occipital Asymmetries and Structural Changes identified by MRI

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Purpose
To examine the relationship between VEP trans-occipital asymmetry and MRI findings of the visual pathway.

Methods
We undertook a retrospective review of 11 patients with NF1 who had VEP examinations (minimum of four), showing an initial trans-occipital VEP asymmetry, and MRI scans in the same time frame (median monitoring period of 2 years). VEPs were recorded to pattern reversal (28° field, 3/s reversal 400' to 6.25' minutes of arc), pattern onset (28° field, 3/s onset 400' to 25' minutes of arc) and flash (Grass 4 strobe) from active electrodes at the inion, Oz, O1 and O2 referred to Fz. The differences in the VEP amplitudes recorded at O1 and O2 determined the presence of full field pattern or flash trans-occipital asymmetry. This was confirmed with half field testing in 9/11 patients. An asymmetry was defined as a minimum amplitude difference of 30% for uncrossed asymmetries (hemisphere dysfunction) and a 20% difference in each eye in crossed asymmetries (chiasmal dysfunction). These were compared with the MRIs for each patient.

Results
In 8/11 patients (73%) the VEP asymmetry matched the MRI findings. One patient (of 11) had a consistent uncrossed asymmetry in full field VEPs over time in the absence of any MRI finding affecting the visual pathway directly. Two patients (of 11) had initial asymmetries, regarded as suspicious, which were not confirmed at subsequent recordings.

Two (of 8) patients showed a change in the VEP asymmetry over time. In one patient the VEP improved and this was reflected in a decrease in the tumour bulk. In the second, VEPs had shown a left hemisphere dysfunction, corresponding with a left hemisphere glioma. As this glioma progressed to involve the optic chiasm, so the VEP asymmetry changed to a bitemporal hemanopia. In the remaining 6/8 patients no change was seen in the VEP asymmetry, confirmed by the MRI scans in which the tumours were shown to be static.

Conclusion
Monitoring of trans-occipital asymmetry can be a non-invasive indicator of tumour progression or regression and therefore provides a useful indication of when to have a further MRI scan.
To further understand VEP asymmetries in the absence of conventional MRI findings the future may be to employ tractography to assess the white matter connectivity of the visual pathway.

15:15 – 15:30

The Step VEP Acuity Test in Suspected Functional Visual Acuity Loss

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Purpose
Children presenting with unexplained visual acuity loss without apparent organic disease are often suspected of having functional visual loss. Behavioural acuity testing approximately demonstrates the reported acuity loss. However, pattern VEPs usually remain normal if the loss is non-organic. The step VEP test is a rapid, objective acuity test routinely used in our clinics to measure visual thresholds.

Methods
A retrospective audit was conducted to assess the utility of the step VEP acuity test in the diagnosis and management of patients with suspected functional vision loss. The most recent 29 patients fulfilling the following criteria had their medical notes reviewed: suspected functional visual impairment; reduced VA as assessed by optician/ophthalmologist/orthoptist using behavioural techniques; normal full-field ERGs.
Results: Of these 29 patients, 23 (79%) had normal step VEP results and six (21%) had abnormal step VEP results. 22 of the 23 patients with normal step VEPs had no evident ophthalmological cause for poor vision and eventually reported resolved or resolving acuity. Five of the six patients with abnormal step VEPs were diagnosed with Stargart macular dystrophy, optic nerve hypoplasia (N=3) or craniopharyngioma. These results indicate 96% sensitivity and 83% specificity for the step VEP in detecting functional vision loss.

Discussion
This small sample demonstrates the utility of the step VEP in distinguishing organic from non-organic causes of acuity loss in children. The test need only be performed once at the initial presentation. This early and robust piece of evidence has two potential benefits: firstly, management by reassurance when no organic cause is suspected has a better prognosis if the reassurance intervention is prompt. Secondly, if the step VEP test suggests an organic cause, less time need be spent ruling out functional loss using subjective techniques and more rapid intervention can be offered for the organic cause.

Acknowledgement: Dr AM Mackay for her work in developing the step VEP.

15:30 – 15:45

Light Pipes in the Retina

Malcolm Brown

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Have you ever wondered about the photoreceptors being at the back of the retina, so that light must travel through the various cell and fibre layers before detection? Surely these layers must cause scattering of the light resulting in blurring similar to placing a translucent material in front of an object.

In this talk we learn of new research showing that the structure of the retina includes special adaptations to keep the final image sharp.