ARVO EDUCATION COURSE

Saturday, April 27, 2019
8:30am-4:30pm
Vancouver Convention Centre
Vancouver, British Columbia, Canada

Applying electrophysiological techniques to translational vision research

Course organizer

Mitchell G Brigell, PhD FARVO, VP Clinical Development, Aerpio Pharmaceuticals

Presentations

Presenters and presentations may change.

8:30-8:45am

Welcome and introduction
Mitchell G Brigell, PhD FARVO

This presentation will briefly introduce technical aspects of ERG recording and characteristics that make the ERG an excellent tool for translational research.

8:45-9:15am

Cellular Origins of the electroretinogram
Laura Frishman, PhD, FARVO, University of Houston

The electroretinogram (ERG) is an electrical potential generated by the retina of the eye in response to light. It can be recorded noninvasively, using electrodes placed on the cornea, and it reflects the summed response of all the cells in the retina. It is useful tool for assessing the functional integrity of the retinal cells and circuits. The ERG arises from extracellular currents that flow in the retinal tissue as a result of neuronal signaling and in certain cases spatial buffering of potassium by glial cells. This lecture will define the specific neuronal and glial origins and mechanisms of generation of the various waves of the dark, and light-adapted ERG.

9:15-9:45am

Using electrophysiology to probe the visual cycle
Omar Mahroo, MD, PhD, University College, London

The talk will discuss methods of probing kinetics of dark adaptation and photopigment bleaching and regeneration in rod and cone pathways, in the human eye in vivo, using the full-field electoretinogram (ERG). By delivering flashes before and after bleaching exposures, and measuring ERG amplitudes (measured at peak or at a fixed time following flash delivery) dynamics of changes in retinal sensitivity can be quantified. With several assumptions, and by taking into account response-intensity relationships in the pre-bleach dark-adapted state, these non-invasive measurements can be used powerfully to probe recovery of circulating current and photopigment in rod and cone photoreceptors, as well as the gain of phototransduction. Comparisons will be made with retinal densitometry (which provides a direct measure of photopigment levels) and psychophysical data.

9:45-10:15am

Using visual electrophysiology to understand disease and the impact of therapy

Graham Holder, PhD, University of Singapore

The presentation will address the use of electrophysiological investigation in the clinic. Interpretation of electrophysiological signals involves an understanding both of the origins of the signals and of the relationship between the electrophysiological data and the underlying pathophysiology of the disease. A case-based approach will be used to illustrate these points both in inherited and acquired disease. Appropriate imaging (optical coherence tomography, fundus autofluorescence imaging etc.) will be incorporated to provide a fully integrated approach to patient investigation and care.

10:15-10:45am

Application of visual electrophysiology in models of retinal degeneration

Simon Petersen-Jones, Michigan State University

Animal models play an important role in the investigation of the pathophysiology of retinal degenerations as well as the development of therapies for these conditions. Models range from zebra fish and laboratory rodents to large animals including cats, dogs, pig, sheep, chickens and primates. The models may have spontaneous inherited retinal degenerations or may be engineered models. Electroretinography plays a major role in the study of these models as well as in the assessment of the efficacy of therapeutic interventions. This presentation will briefly describe electroretinographic recording from specific animal models to allow the investigation of retinal dysfunction and give examples of electroretinography used to assess therapeutic outcomes.

10:45-11am

Questions and Answers

11-11:15am

Break

11:15-11:45am

Electrophysiological outcome measures in therapeutic trials for retinal degeneration

Mark Pennesi, MD, PhD, Oregon Health Science University

This presentation will review the challenges associated with using electrophysiology (ERG and multifocal ERG) as endpoints in clinical trials.

11:45am-12:15pm

Use of visual electrophysiology to detect neurodysfunction in models of diabetic retinal disease

Machelle Pardue, PhD, FARVO, Georgia Tech

Diabetic retinopathy is a leading cause of vision loss in adults. Current treatment options focus on late stage vascular abnormalities. However, early stage neuronal dysfunction has been identified using

electroretinography (ERG) and might provide an opportunity for early detection and treatment. This talk will review data from diabetic animal models and humans that show delays in ERG oscillatory potentials in response to dim flash stimuli prior to vascular structure changes. Early detection of diabetic retinopathy opens a new treatment window. Neuroprotective approaches for diabetic retinopathy that slow the progression of vision loss will be discussed, such as dopamine treatments and physical exercise.

12:15-12:30pm - Questions to speakers from the morning session

12:30-1:30pm - Lunch (one-hour)

1:30-2pm

The use of visual electrophysiology in vascular retinopathy/optic neuropathy

Mary Johnson, PhD, University of Maryland

Reduced vascular perfusion to the optic nerve can be idiopathic (non-arteritic anterior ischemic optic neuropathy; NAION) or result from vascular thrombosis of the posterior ciliary arteries or pial vessels due to temporal arteritis (arteritic anterior ischemic optic neuropathy; AAION.) The loss of blood flow results in infarction of the optic nerve near the lamina. The VEP amplitude is reduced, often profoundly, in these patients, while VEP latency is typically unaffected. For this reason, the VEP can be useful in differentiating between NAION and acute optic neuritis, which produces large latency delays. In NAION, the pattern ERG (PERG) and ERG photopic negative response (PhNR) have been shown to reflect abnormalities in the proximal retina in the affected eyes of patients with NAION. The PhNR has revealed functional loss in some unaffected, fellow eyes of these patients, perhaps reflecting subclinical pathology, an interesting observation given that the risk for involvement of the fellow eye is 5% per year.

Unlike optic nerve hypoxia, reduced perfusion to the retina may result in either infarction or in partially perfused tissue that is still responsive but not normal (i.e. ischemic). Infarction produces ERGs with reduced amplitudes and ischemia produces ERGs with delayed timing. Thus, unlike fluorescein angiography, the ERG can determine if non-perfused tissue is infarcted or ischemic, and the difference is important because the degree of ischemia is the best predictor of proliferative retinopathy. ERG changes in sickle cell retinopathy, branch and central retinal vein occlusion, central retinal artery occlusion, ocular ischemic syndrome and diabetic retinopathy will be discussed with regard to the mechanisms of retinal function loss and how this information is important in managing patients.

2-2:30pm

Application of visual electrophysiology to glaucoma models

Bang Bui, PhD, University of Melbourne

Electroretinography has become a mainstay measures of vision function for glaucoma researchers. Its application to animal models of glaucoma have helped to elucidate pathophysiological processes. The purpose of this presentation is to: (i) describe applications of the full filed electroretinogram (ERG) to further our understanding of retinal changes induced by acute and chronic intraocular pressure elevation, (ii) consider how blood pressure and intracranial pressure influences how the ERH is affected by IOP elevation and (iii) explore how quantifying ERG recovery following IOP elevation provides a sensitive index of the capacity for the visual system to cope with stress.

2:30-3pm

Electrophysiologic measures of retinal ganglion cell dysfunction in glaucoma

Vittorio Porciatti, DSc, FARVO, University of Miami

The electrical activity generated by retinal ganglion cells (RGCs) and their axons is recordable with different ERG modalities, among which the Pattern ERG (PERG) in response to contrast-reversing patterns is the best known and understood. The PERG reflects the spatial, temporal, and chromatic properties of RGCs and it is readily recordable in human and experimental animals with high signal-to-noise ratio. The PERG is altered when RGCs are either degenerated or still alive but dysfunctional. In glaucoma, PERG loss may be reversible after treatment after IOP-lowering treatment. Progressive PERG loss in glaucoma-prone subjects precedes loss of retinal nerve fiber layer thickness by several years, and PERG progression may be hindered after IOP lowering. PERG loss may be inducible in susceptible eyes of glaucoma suspects upon head-down posture, which may predict future RGC loss. PERG provides unique information, complementary to OCT imaging and Visual Field, which may help in glaucoma diagnosis and management. The presence of comorbidities such as cataract ad diabetes may nonspecifically alter the PERG.

3-3:15pm

Afternoon Break

3:15-3:45pm

Application of visual electrophysiology to understanding development of the visual system

Ann Fulton, MD, FARVO, Childrens Hospital Boston

Application of visual electrophysiology to understanding development of the visual system. Electroretinography and the visual evoked potential have characterized normal development of the human visual system from quantum catch by the photoreceptors in the retina to processes in the central visual pathways. An overview of the non-invasive procedures will be presented and the concepts underpinning interpretation of pediatric visual electrophysiology data that impact translational vision research will discussed.

3:45-4:15pm

Application of visual electrophysiology in pediatric ophthalmology

Scott Brodie, MD, PhD, FARVO, NYU-Langone Medical Center

Summary with examples of major applications of techniques of clinical electrophysiology of vision (VEP, ERG, and occasionally, EOG) to visual disorders of children.

Visual Evoked Potentials (VEP)
Normal development of the VEP
Recommendations for timing of VEP testing
Perinatal brain injury (“cortical blindness”)
Meningitis
Assessment of equivalent “visual acuity”

Amblyopia?
Albinism
Demyelinating disease (optic neuritis, retrobulbar neuritis)

Electroretinogram (ERG)
Normal development of the ERG
Congenital poor vision with nystagmus
Leber congenital amaurosis
Achromatopsia
Congenital stationary night-blindness
Juvenile (X-linked) retinoschisis
Albinism (and other forms of foveal hypoplasia)
Primary motor nystagmus
Retinitis Pigmentosa and similar disorders
Inheritance patterns:
X-linked
Autosomal recessive
Autosomal dominant
"Berson's Rule"
Choroideremia
Gyrate Atrophy
Stargardt disease
Monitoring drug toxicity
Vigabatrin (Sabril)
Ophthalmic artery chemotherapy ("chemosurgery") for retinoblastoma

Children with normal ERGs and VEPs
"Delayed visual maturation"
Refractive errors
Malingering and other non-organic visual loss.

Electro-oculography (EOG)
Require sustained cooperation x 30 minutes
Rarely used with children
Best disease
Other disorders of the RPE
Pattern dystrophies

4:15-4:30pm

Questions for Afternoon Speakers