

**SOE2017**



**EUROPEAN SOCIETY OF OPHTHALMOLOGY  
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## **Course C21**

# **Visual Electrophysiology in Children**

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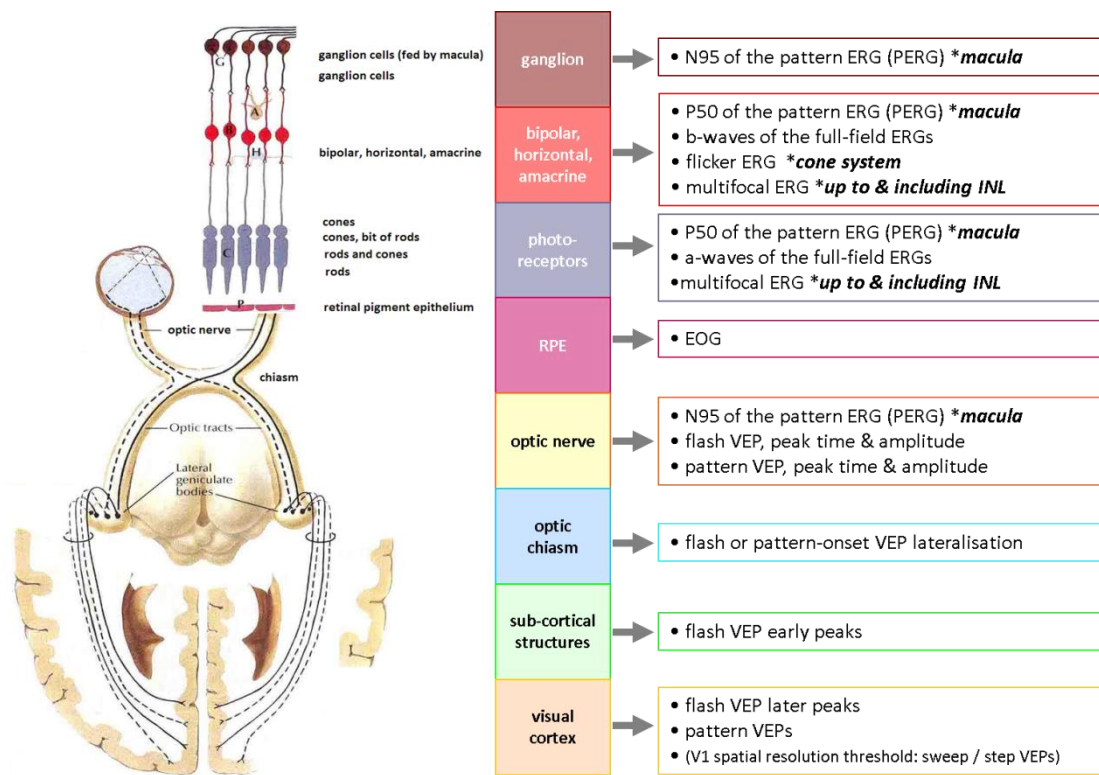
16:15 - 17:45 hrs

Room 118/119

## **HAND-OUTS**

## Introducing visual electrophysiology tests and results – Ruth Hamilton

- A description of paediatric tests and how response mature



Ruth Hamilton, SOE 2017

### Maturation of visual electrophysiological measures

As with all physiological measurements, it is essential to know what a normal VEP, ERG, PERG, mfERG or EOG looks like. Acquisition of normative data is required by the Standards of the International Society for Clinical Electrophysiology of Vision in order to provide decision limits for a test outcome parameter. The rapid maturation of the visual system in the earliest years of life makes collection of electrophysiological normative data a substantial undertaking.

ERG maturation comprises shortening peak times and increasing amplitudes of its constituent waves, reflecting retinal neural and vascular tissue development. Retinal maturation remains incomplete at birth: photoreceptor outer segments are scarcely half their adult length, and the fovea remains poorly formed, still containing inner nuclear layer neurons. Rod-system sensitivity at birth as measured by the ERG is around 0.6 log units poorer than adult sensitivity, and ERG maximal amplitudes are only around 10% of adult values. Sensitivity matches adult values by 6 months while amplitudes reach adult values by 12 months. Cone-system ERGs show faster maturation than rods.

The pattern ERG peak times are adult-like by around 6 months, and amplitudes peak at around 6 years of age.

The multifocal ERG in 10-week infants has amplitudes around half those of adults, with slower peak times; over 10 years of age, there is a reduction of amplitude and increase of peak times of first- and second-order components: few data are available for intermediate ages. Premature birth, even in the absence of retinopathy of prematurity, confers functional deficits which persist into childhood.

VEP maturation reflects maturation of the fovea and the visual pathways. The fovea remains immature at four years, while myelination in the optic nerve and tracts is not mature until around 5 years. In the lateral geniculate nucleus and cortex, dendrites and spines increase in number during the first postnatal months before decreasing to adult-like levels by the second year. Similarly, cortical synaptogenesis is rapid after birth, being maximal at about 8 months before being pruned to reach adult-like numbers at about 11 years. Parvocellular pathways mature more rapidly than magnocellular pathways. The flash VEP at birth is a simple, slow deflection, which rapidly develops complex morphology during the first six months. Early components become adult-like by one year, but later components remain immature until after five years of age. Transient pattern reversal VEPs, originating in the primary visual cortex, are evident from birth providing the pattern size can be resolved. For 60' checks (0.71 cpd for the fundamental spatial frequency), peak time of P100 reduces sharply from >200ms in the first weeks of life to an adult-like 100ms by 12 months of age. Amplitude generally increases but is highly variable. Maturation is slower for smaller patterns. Steady-state VEPs can be used to measure spatial frequency VEP threshold, which improves from around 5 cpd in the first month to 10 cpd or better by 6 months of age.

The multifocal VEP has been investigated a little in normal paediatric populations, and shows increasing amplitudes and reducing peak times up to 13 years of age.

Summary:

- ISCEV standard protocols can be modified for children
- Maturation means you need age-stratified reference data
- Cone, and mixed rod-cone ERGs are adult-like by the second year
- Rod-only ERGs are adult-like by school-age
- PERGs are adult-like from 6 months
- MfERGs are immature at 10 weeks: adult-like by school-age
- EOG Arden ratios are adult-like from infancy
- Flash VEP: adult-like by school age
- Pattern VEPs (60') during the second year
- Pattern VEPs (15') during the third year

## **Indications for visual electrophysiological tests...**

Marta Pawlak 10 mins

*Clinical signs and symptoms that prompt referral.*

There's a variety of additional examinations in the hands of an ophthalmologist that help in solving clinical problems and lead to the final diagnosis. Many of them show the anatomy of the eye or the visual pathway. However, the electrophysiological tests give the objective information of the visual pathway function.

Visual electrophysiological tests include: visual evoked potentials (VEP), electroretinography (ERG), electrooculography (EOG), pattern electroretinography (PERG) and multifocal electroretinography (mfERG). In a paediatric patient, though, the compliance is a limiting factor in choosing the examinations combination.

Classical indications for visual evoked potentials (VEPs) include: congenital abnormalities of the optic disc; hereditary optic neuropathies; demyelinating, inflammatory, infectious and infiltrative optic neuropathies; optic chiasm dysfunction. Classical indications for electroretinography (ERG) include: retinal dystrophies (cone/rod/macular), night blindness, choroidal dystrophies, vitreoretinopathies, toxic damage, intraocular foreign body.

However, what we face in everyday clinical practice is the patient's/ the patient's parents' complain: no eye contact, poor fixation or specific clinical finding that needs further investigations: pale optic disc, nystagmus, decreased visual acuity with normal eye fundus, unilateral decreased visual acuity that does not improve with patching therapy, sudden visual acuity decrease.

Clinical cases along with the results of additional examinations performed and clinical reasoning leading to final diagnosis will be presented.

The list of ocular diseases associated with nystagmus in childhood will be discussed.

The analysis of the causes of poor eye contact in infancy will be presented based on the author's experience.

Visual electrophysiological tests are of a great importance for a paediatric ophthalmologist. They help with the early diagnosis thus enabling the prognosis, orientation of genetic examination and counselling as well as providing adequate psychomotor development stimulation.

## **What electroretinography (ERG) tells us.**

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SOE Course in Paediatric Electrophysiology, Barcelona, June 2017.

Electrophysiological testing provides an objective and non-invasive method for visual pathway evaluation. Electrophysiology therefore has a privileged position in the child with retinal disease, who may not accurately be able to describe their symptoms. It enables the distinction between disorders that may present with similar signs and/or symptoms and facilitates the differentiation between benign or severe, progressive or stationary disorders. Complementary use of different electrophysiological procedures allows accurate characterisation and localisation of dysfunction. For example, EOG reflects the function of the photoreceptor/RPE interface; the ERG, rod and cone photoreceptor and inner retinal function; the PERG, macular function and central retinal ganglion cell function; and the VEP intracranial visual pathway function. It should always be remembered that VEP delays and abnormalities are non-specific and that VEP delays are commonplace in eyes with macular dysfunction. Such eyes may have normal structural imaging; normal structure does not mean normal function! Electrophysiological phenotyping has become increasingly important as the ability to genotype has increased; accurate phenotyping can facilitate focused molecular screening in patients with atypical features. Equally, the objective data provided by ERG is used both as an outcome measure and as an index of safety in clinical trials of novel therapeutic interventions.

The techniques for recording ERGs in young children and infants will be described, along with those used in older children and adults, and clinical examples shown to illustrate the diagnostic value of ERG in various disorders, both inherited and acquired. For example, the findings in retinitis pigmentosa (rod-cone dystrophy), commonly associated with nyctalopia, will be compared

and contrasted with those of congenital stationary night blindness. The former, being caused by photoreceptor dysfunction, shows reduced dim flash ERGs (rod-specific, DA 0.01) accompanied by marked a-wave reduction in the bright flash dark-adapted ERG (DA 10.0); the latter also shows reduced dim flash ERGs (rod-specific, DA 0.01), but the bright flash dark-adapted ERG (DA 10.0) contains a normal a-wave but a reduced b-wave (a “negative” or “electronegative” ERG waveform), confirming normal photoreceptor function and establishing inner retinal dysfunction. A further disorder associated with night blindness, fundus albipunctatus (RDH5 mutation), will be used to illustrate not only the power of electroretinography to reveal the pathophysiological mechanisms underlying the disease, but also the need always to consider the underlying pathophysiology when interpreting ERGs and when determining whether the ISCEV Standard ERGs, a minimum data set, can actually answer the clinical question. Another disorder often associated with night blindness is vitamin A deficiency. An example of this will be shown, which will illustrate the ability of the ERG not only to make the diagnosis but also objectively to assess the response to treatment.

The combined role of pattern and full-field ERG in the assessment both of macular and global retinal function will be discussed; the full-field ERG is normal when dysfunction is confined to the macula. The concept of “diagnostic” or pathognomonic ERGs will also be addressed.

## Visual Electrophysiology in Children

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### What the VEP can tell us

The objective nature of the VEP makes it a **‘GO TO’ test** for young children and adolescents.

VEPs, in combination with ERGs, can

- i) indicate where in the visual pathway a problem lies and
- ii) suggest what may be possible in terms of vision

Some clinical applications in paediatric practice are described below.

### Investigate functional, or medically unexplained, visual loss

VEPs reflect the central field. The PVEP to 60' checks tolerates ~ 8D blur, the PERG is sensitive to ~ 0.5D blur. Simultaneous recording of a PVEP and PERG can distinguish between defocus, maculopathy or macular pathway dysfunction as a cause of visual loss.

### Localise visual pathway dysfunction

Monocular, multichannel VEPs combined with ERGs functionally dissect the visual pathway.

*for non-seeing infants* localise dysfunction to retina, optic nerves, chiasm or hemispheres *for infantile nystagmus* assess function of the anterior sensory pathway, e.g. the ERG will identify severe rod/cone or cone dysfunction, CSNB and the VEP, optic nerve hypoplasia, albinism or chiasmal hypoplasia.

### Suggest visual potential of children unable to make a behavioural response

A robust PVEP to a small check size in a child with CVI provides an optimistic prognosis that the striate cortex can support good vision if the association areas are healthy and functional.

### Monitor visual development from birth

PVEPs help plan the timing of intervention e.g. surgery for congenital cataracts. PVEPs to a range of check sizes, (smaller and larger than the ISCEV recommended 60' and 15'), can monitor maturation of the visual pathway from birth. PVEPs appear earlier to larger checks than to smaller checks and 'p100' latency matures by 7 months of age to the larger checks 100'. Maturation changes continue throughout life and comparison with age appropriate reference data is important. NB infants with isolated DVM have normal latency VEPs.

### Monitor consequence of disease and treatment on visual pathway function

Serial comparison with an individual baseline VEP is important e.g. hydrocephalus, glioma, or neuritis. Inter-individual variability of VEPs is most for flash VEPs and least for reversal VEPs. If there is optic atrophy a reversal VEP can have two peaks; the earlier latency peak must not be interpreted as maturation. If an enlarged blind



spot encroaches on the central half field it will alter the occipital distribution of the full field monocular PVEP.

### Monitor preservation or loss of the central macular field

PVEPs indirectly characterise macular involvement in rod /cone retinal dystrophies or can indicate the extent of macular function in retinoblastoma during IAM treatment.

### Limitations of interpretation

**Seizures:** The VEP is extracted from the EEG. The VEP occurs at a fixed time after the visual stimulus. By averaging lots of trials the time locked VEP emerges from the random background EEG which is cancelled. Some non-seeing infants, typically without nystagmus, have such large and intrusive background that the pVEP cannot be detected.

**Association areas:** A VEP cannot tell us if signals arriving at the striate cortex are used by the rest of the brain to 'see' or recognise the visual world. In cases of lissencephaly, for example, the PVEP is normal for age, but the child remains non-seeing because the association areas cannot further process information in the striate cortex for seeing.

**Clinical context:** A VEP is a snapshot in time and should be interpreted in the full clinical context to extract maximal clinical value.

### General notes about VEPs for children

A pattern VEP is dominated by the macula representation of the occipital cortex which is expanded in the striate cortex V1 closest to the surface electrodes. A pVEP is generated by the function of only a few central few degrees of visual field. A large stimulus field (~30degrees) will ensure adequate macular stimulation even if a child's fixation wanders.

VEP recording in children is very robust. Normal VEPs in children are large amplitude. A pattern VEP can be recorded if a child's eyes are aligned with a reversing or appearing check display using corneal reflection. A flash stimulus can stimulate even if the baby's eyes are closed. The pattern reversal VEP is relatively insensitive to defocus. Pattern onset stimulation can be used in cases of active defocus or unstable eye movements such as nystagmus in place of reversal VEPs. Both flash and pattern onset stimulation are required to detect the chiasmal misrouting of albinism. The flash VEP is more sensitive in younger infants and pattern onset VEPs in older children. As a rule all three stimulus modalities should be applied in each child to provide overlapping complementary information.

### Intra-individual repeatability of electrophysiology findings - examples

ERG: Hamilton R et al Docum Ophthalmol 2015 130:83-101

PVEP: Mellow T et al Docum Ophthalmol 2011 122:133-139

PVEP: Sarnthein J et al 2009 Clin Neurophysiol 2009 120:1835-40

### How to do a VEP – the ISCEV standard

Odom, J.V., Bach, M., Brigell, M. et al. ISCEV standard for clinical visual evoked potentials: (2016 update) Doc Ophthalmol (2016) 133: 1, pp 1-9