ELECTRODIAGNOSIS

Achieving objective

Peter Good explains the use of the steady state pattern electroretinogram in the diagnosis and management of glaucoma and the development of the Diopsys electrodiagnostic system which brings the science to the community practice

Measurements of retinal ganglion cell (RGC) complex and retinal nerve fibre layer (RNFL) thicknesses are important in the diagnosis and management of glaucoma. Use of the OCT has played an important role in making these measurements available, and there are a number of algorithms that identify change and progression in order to identify glaucomatous damage to ganglion cells or thinning of the RNFL.

However, by the time significant measurable loss of RGC occurs, and therefore glaucomatous optic neuropathy can be diagnosed, irreversible visual functional loss will have occurred. This in turn may result in permanent field loss (figure 1).

Therefore, using current diagnostic methodology, treatment may only commence when up to 80% of RGC have already disappeared. How useful therefore would be a diagnostic test that identifies glaucomatous RGC damage before cell death and therefore permanent functional loss occurs?

OCULAR ELECTROPHYSIOLOGY

Ocular electrophysiology is normally not suitable for the diagnosis of glaucoma. Outer retinal function can be determined by the flash electroretinogram (ERG), whilst optic nerve function can be determined by the high contrast pattern visual evoked potentials (VEP). However, neither will be abnormal in glaucoma except the VEP in advanced disease. In glaucoma, it is now established that RGC dysfunction and subsequent apoptosis precedes axonal loss. RGC dysfunction can be measured using the pattern ERG (PERG) n95 component,[1] but the transient pattern ERG (PERG) can be difficult to obtain, due to the need to use corneal contact electrodes which can obscure the stimulus and are susceptible to movement artefact and are often not repeatable. They also measure too expansive an area of RGCs to pick up early glaucoma. Furthermore, recordings of transient PERG are normally only available in specialist electrophysiology laboratories. This technique is therefore not suitable for screening for glaucoma or monitoring disease progression. Multifocal VEP can identify potential field loss in glaucoma objectively, but has poor specificity.

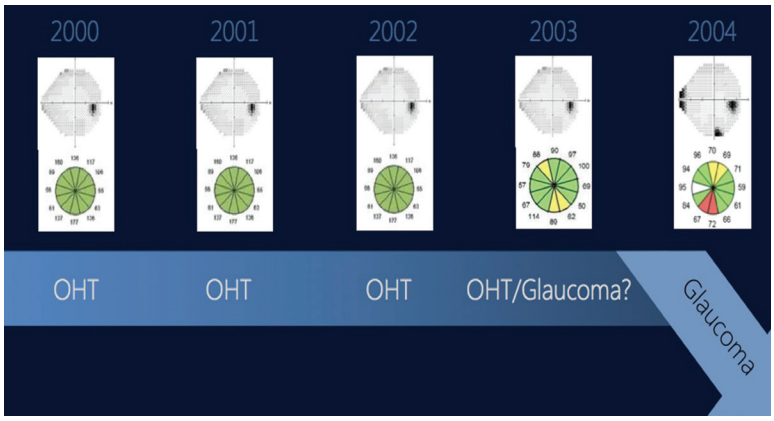


FIGURE 1 Glaucoma detected after RGC loss will typically go on to develop perimetric loss

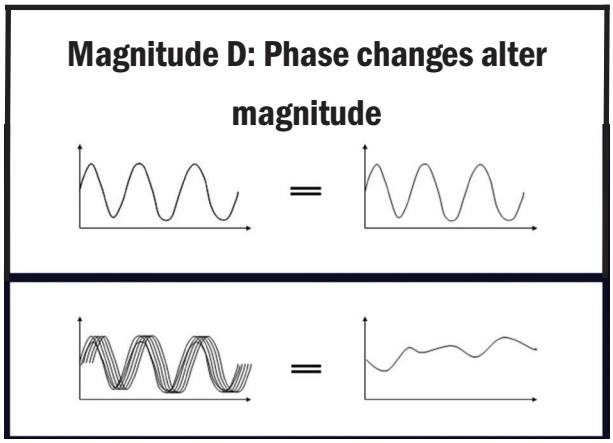


FIGURE 2 Effect of phase change on the magnitude of the averaged SSPERG

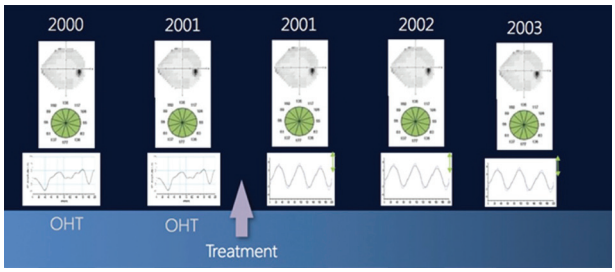
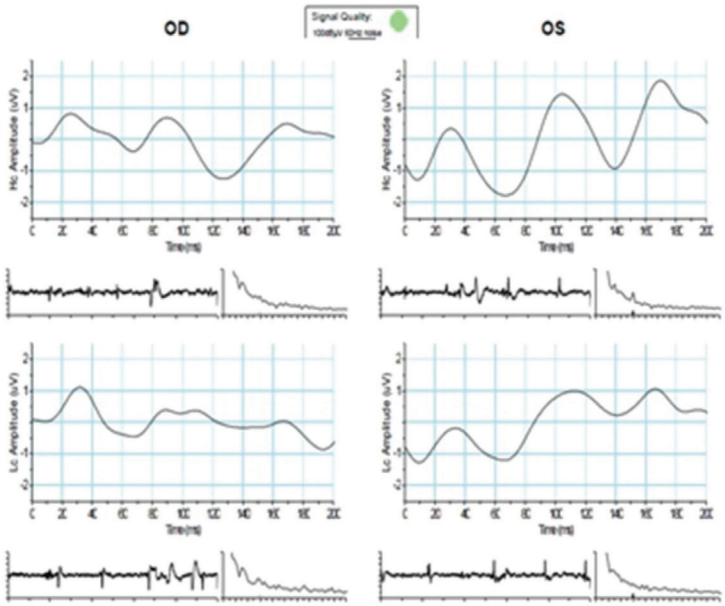


FIGURE 3 DiopSys pERG may detect disease and prompt treatment before RGC loss and permanent neurological damage has been established

FIGURE 4 The DiopSys non-invasive electrode (top) for use with the DiopSys systems (below)



Parameter	OD Hc	OD Lc	OS Hc	OS Lc
Magnitude (uV)	1.23	1.13	1.50	0.90
MagnitudeD	0.60	0.51	1.25	0.61
MagD/Mag Ratio	0.49	0.45	0.84	0.68
SNR (dB)	1.8	0.6	4.5	1.1
Artifacts	1	4	2	1

FIGURE 5 This patient has glaucoma in the right eye. The DiopSys pERG report links to a normative database and the 'traffic light' system aids the clinician interpretation in highlighting data outside the expected normative values (in yellow and red)

STEADY STATE PERG

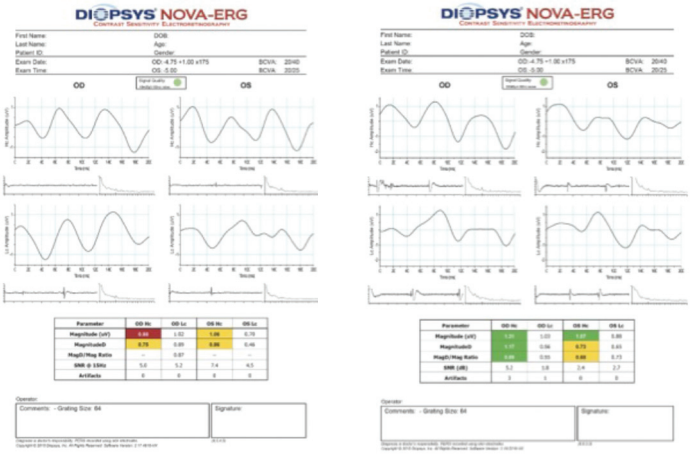
Steady State PERG (SSPERG) utilises high frequency (>10 Hz) pattern stimuli (high spatial frequency grating) to provide a sinusoidal waveform which consists of multiple n95 components. The magnitude and phase of the response can be used to determine RGC function using frequency analysis. High frequency pattern stimulation of the retina causes increased blood flow to the RGC and results in increased oxygen consumption and changes in autoregulation effectively stressing the ganglion cells.[2] This potentially causes the RGC to become physiologically exhausted and will potentially reduce their function. Healthy ganglion cells recover quickly which results in a normal SSPERG. If the ganglion cells are unhealthy, as in glaucoma, then the recovery process is delayed and the SSPERG shows reductions in magnitude or changes in phase.[3] One of the first signs of RGC abnormality in the SSPERG is variability in the phase of the response. This variation in phase will ultimately lead to a reduction in the magnitude of the averaged response (figure 2). It has also been shown that reducing the intra ocular pressure in ocular hypertensive patients can increase the SSPERG amplitude over a period of a few weeks.

Studies have shown that abnormalities in SSPERG can occur with or without RNFL or RGC defects on OCT and will normally precede RGC or RNFL loss by several years. What is also encouraging is that SSPERG abnormalities are reversible and a number of studies have shown that if pressure lowering treatment is introduced when the SSPERG is abnormal, without changes in the OCT, then the SSPERG can recover and RGC loss prevented (figure 3).[4]

DIOPSYS

Whilst SSPERG technology has been around for a decade it has not been incorporated into a commercially available device. The Diopsys company have developed an electrodiagnostic system which has the potential to be used for screening purposes. This system incorporates a built in stimulating and recording device on a portable platform. SSPERG at 15 Hz frequency and 24 degree stimulus field, are recorded using a unique bipolar lid electrode (figure 4).

Recordings of pattern reversal VEP, flicker ERG and SSPERG can be made at varying stimulus parameters (high and low contrast and 24 and 16 degree stimulus area). With the SSPERG protocol measurements of magnitude (MAG), phase consistency (MAGD) and how the phase changes are affecting magnitude (MAGD/MAG) are determined. In glaucoma, 96% confidence intervals (yellow flag) and 98% confidence intervals (red flag) show changes in MAG, MAGD and MAGD/MAG ratio due to variations in phase. These values reflect abnormalities in RGC function and have a high specificity for glaucomatous RGC damage. The Diopsys electrodiagnostic system can help differentiate between RNFL and RGC defects in glaucoma and other optic neuropathies or optic disc anomalies defects; including nutritional amblyopia, and myopic peripapillary atrophy. Specificity can be improved by utilising the pattern VEP in the Diopsys system. The VEP can recorded using high contrast (parvocellular pathway) or low contrast (magnocellular pathway) stimuli. Glaucoma causes changes principally in the magnocellular pathway, whereas most other optic neuropathies principally affect →



Abnormal magnitude RE & borderline LE

Two months later IOP decreases to 16mmHG R&L

FIGURE 6 Sixty-year-old female patient with reduced SSPERG (left) and intraocular pressures of 24mmHg both eyes. After selective laser trabeculoplasty, the pressures were 16mmHg and the SSPERG shows recovery (right)

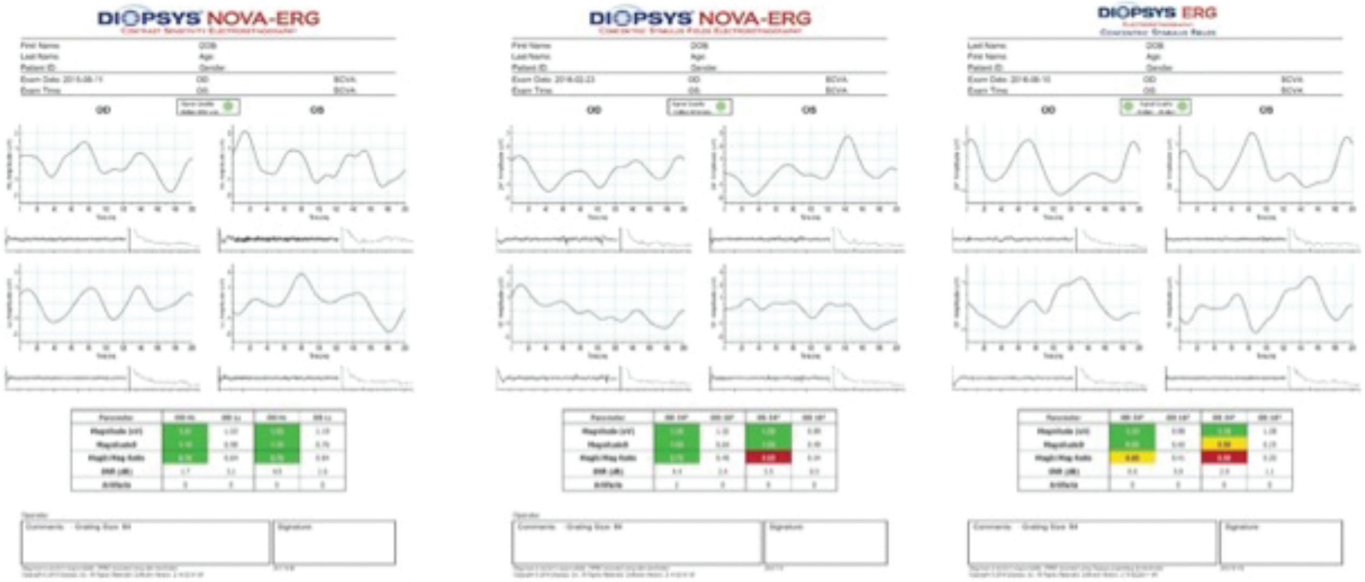


FIGURE 7 A patient with normal SSPERG but pressures of R20mmHg and L27mmHg on initial examination. After repeated six monthly monitoring, the SSPERG is shown to become abnormal

the parvocellular pathway.

For the first time there is a commercially available objective test to help diagnose glaucoma in its earliest stages, potentially before permanent loss of ganglion cells or nerve fibres occur. SSPERG measurements using the Diopsys system appear to be a means of diagnosing early and reversible RGC changes in glaucoma.

The technique has applications as a screening tool, and in monitoring the progression of the disease, as well as assessing the effectiveness of pressure lowering treatments. It can help decide which patients with ocular hypertension require treatment. The Diopsys system is easy to use and does not require electrodiagnostic expertise or technical knowledge since the Diopsys lid ERG electrode is easy to apply. The coloured flag system of recording abnormality removes the need for a specialist in ocular electrophysiology to interpret the findings whilst still giving numerical values in order to monitor progression or recovery of ganglion cell function (figures 5, 6 and 7).

The Diopsys system also provides Ganz field flicker ERG for assessing central retinal and macular function. It is therefore a fully functioning portable office based electrodiagnostic system ideal for use in the optometric setting.

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4 Parisi V, Colacino G, Milazzo G, Scuderi AC, Manni G: Effects of Nicergoline on the retinal and Corticasl Electrophysiological responses in glaucoma patients: a preliminary open study:*Ophthalmology* 2005: 112: 20-27

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