INTRODUCTION

Globally, it is estimated that 1.1 billion people are visually impaired, including 43 million people who are blind [1]. Prevalence of visual impairment is estimated as 1.0% and blindness as 1.7% according to recent studies done in Sri Lanka [2]. Most of the visual disorders resulting in significant visual impairment and blindness are due to lesions in the optic nerve and retina. It has been identified that 90% of this visual impairment is avoidable if detected and treated as early as possible. Though there are many sophisticated techniques to assess the structural integrity of the visual pathway, there are only a very few methods available to assess the functional integrity. To date, visual electrophysiology is the key test used to assess the functional integrity of the visual pathway objectively.

Clinical electrophysiological testing of the visual system incorporates a range of non-invasive tests and provides an objective indication of function related to different locations and cell types within the visual system. Though visual electrophysiology is considered as an essential part of battery of visual tests done in other countries in the world, this does not seem to play a major role in the ophthalmology field in Sri Lanka up to now.

The present work is based on the advanced visual electrophysiological techniques and many other collaborative studies carried out at the Neurophysiology Unit, Teaching Hospital, Peradeniya. The primary goal of these studies was to elucidate the changes in visual electrophysiological parameters in different retinal and optic nerve disorders. These studies included patients with optic neuritis, retinal disorders, organophosphorus poisoning and early diabetic retinopathy. Further, there was an interventional study to evaluate the efficacy of the original “Optic Neuritis Treatment Trial (ONTT)” corticosteroid regimen in optic neuritis patients. In addition, a study using healthy normal adults was done to generate normative data. Findings of these studies could be considered as a pioneering collection of research done in the South Asian region to provide many conclusive findings and may be the first study series in the world to address visual electrophysiological data of different visual disorders by a single unit.
METHODOLOGY

Techniques used in these studies included three types of advanced visual electrophysiological tests namely, pattern reversal visual evoked potentials (PRVEP) to assess the functional integrity of the post retinal pathways, pattern electroretinography (PERG) to assess the functional integrity of the macula region and electro-oculography (EOG) to assess the functional integrity of the retinal pigment epithelium (RPE). These were performed in all the participants in all the study groups. Methodology used in these techniques adhered to the latest International Society for Clinical Electrophysiology of Vision (ISCEV) guidelines. Natus EMG/NCV/EP (USA) machine was used to record PRVEP and EOG and Nicolet Viking Quest EMG/NCV/EP machine (USA) was used to record PERG.

Construction of a basic, low cost Ganzfeld dome

Ganzfeld dome which is an essential equipment to perform EOG test was designed and constructed in the workshop of the Faculty of Medicine, University of Peradeniya in collaboration with the Department of Electrical and Electronic Engineering in the Faculty of Engineering, University of Peradeniya adhering to international standards (Figure 1).

RESULTS AND DISCUSSION

Some of the major results of these extensive research studies are given below.

1. Optic neuritis in Sri Lanka- Is it different from typical optic neuritis seen in Western countries?

Typical demyelinating optic neuritis is associated with multiple sclerosis. Clinical profile of optic neuritis in Asia is said to be different from classic Western type optic neuritis. But only a few studies have been done in Asian countries in this regard. In the present study, clinical features of ninety patients with their first episode of optic neuritis were recorded and analyzed with the aim of studying the pattern of clinical profile of optic neuritis in the Sri Lankan population. Interestingly it was noted that our clinical profile is similar to the Asian type optic neuritis with regard to the high occurrence of optic disc edema in fundoscopy (66.7%), preponderance of bilateral occurrence (41.1%) and low occurrence of eye pain (58.8%) at presentation compared to the Western type. Understanding of this different clinical pattern of optic neuritis in the Sri Lankan population will be of utmost value to deduce the etiology, prognosis and management of optic neuritis patients in the
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future studies. Subsequently, the visual electrophysiological parameters were measured and analyzed in a cohort of optic neuritis patients who had their first episode of optic neuritis.

2. Changes in visual electrophysiology measures in optic neuritis

It is known that PRVEP is a highly sensitive test to detect demyelination in optic neuritis. But the retinal involvement in optic neuritis has not been extensively studied using visual electrophysiology. Thus, ninety patients with a diagnosis of optic neuritis were recruited and tested in this study. In the individual analysis, reduced Arden ratio in EOG was found in 55 out of 90 (61.1%) patients. This shows that RPE exhibits abnormal function in the majority of patients with optic neuritis which is considered to be a novel finding even in the international research field [3, 4]. EOG abnormalities observed in our study could be due to a derangement in the chloride conductance which could have occurred as a result of acute episode of optic neuritis. Furthermore, it was found that ganglion cells of the macula region are also affected in our patients with optic neuritis as indexed by abnormalities in the N95 component of PERG. It supplies evidence for the concept of retrograde degeneration to the ganglion cells occurring in optic neuritis [5].

3. ONTT combined regimen, is it effective in optic neuritis in Sri Lanka? - Assessment of the beneficiary effect using visual electrophysiology

The Optic Neuritis Treatment Trial (ONTT) was conducted in a large sample over a 15-year follow up duration. Given that VEPs were not used as an outcome measure in this ONTT study, or even in other studies done in this regard to assess the efficacy of combined corticosteroid treatment, in our study PRVEPs were used to assess the short-term recovery in patients with optic neuritis who underwent the treatment with combined ONTT regimen. The ONTT combined regimen was; IV methyl prednisolone 1g/day for 3 days followed by 1mg/kg/day oral prednisolone for 11 days followed by a short-term tapering dose regimen. Forty-four optic neuritis patients were recruited for this prospective, follow up study. Two follow up assessments were done; 1 and 3 months after the initial, pre-treatment baseline assessment. In this study, interestingly it was observed that there is a marked trend of improvement in P100 latency values in PRVEP in affected eyes in the ONTT combined regimen treated group immediately one month after the treatment and further improvement was observed in 3 months compared to the conservatively managed group (Figure 2). Thus, this study would be of immense value to confirm the evidence derived from the original ONTT further as shown by the pattern of improvement of visual evoked potentials.

4. Organophosphorus poisoning- Will it affect retina and optic nerve function? Evidence by using visual electrophysiology

Organophosphorus (OP) poisoning is a leading cause of mortality in South Asian region. OPs inhibit acetylcholinesterase (AChE) by phosphorylating that enzyme. The RPE is known to have α7 nicotinic ACh receptors located on the outer microvilli of the RPE [6]. This makes the RPE a potential target in OP poisoning, but only a few human studies have examined RPE deficits in OP poisoning, before we looked into it through this study [7]. Our findings showed that Arden ratio is affected in 37.5% of the OP-poisoned patients which could be due to an increase in ACh activity from the outer segments of the photoreceptors which stimulated the ACh receptors on RPE cells. This interaction probably

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**Figure 2:** Comparison of trend of median P100 latency improvement in affected eyes in ONTT combined regimen treated Group (ONTT+) vs conservatively managed Group (ONTT-) over time period of 3 months in patients with optic neuritis
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has caused changes in ionic conductance in RPE leading to changes in EOG parameters. This early detection of visual abnormalities is important to decide the subsequent management of OP poisoned patients which is still a neglected part in their management protocol.

5. Role of visual electrophysiology to assess early diabetic retinopathy

Early detection and timely treatment are important to avoid serious visual impairment in diabetic retinopathy. A few studies with small samples have assessed the post retinal pathways using PRVEP and macular photoreceptors and ganglion cells using PERG separately. However, none had systematically assessed the retina and post retinal pathways in a combined approach. In our study sample of newly diagnosed diabetes mellitus patients without fundoscopic evidence of retinopathy, 56% of the patients had EOG abnormalities that signified deranged RPE-photoreceptor interactions. It was estimated that one-third to three-fourths of patients with newly diagnosed diabetes mellitus show electrophysiological evidence of RPE dysfunction even before developing clinically evident retinopathy or visual impairment [8]. These findings indicate that visual electrophysiological tests can be utilized as a sensitive tool to detect early diabetic retinopathy before developing fundoscopic changes.

6. Role of visual electrophysiology to detect inherited retinal disorders

Currently in Sri Lanka, the diagnosis of inherited retinal disorders is mainly based on the clinical background. With the limited availability of a proper objective tool in detecting the retinal disorders, it was decided to explore the effectiveness of visual electrophysiology tests in the diagnosis of inherited retinal disorders in Sri Lanka. An observational study was conducted in 55 patients with a provisional diagnosis of Best disease, adult vitelliform macular dystrophy, retinitis pigmentosa, Stargardt disease and nonspecific macular dystrophy. It was obvious that parameters of PERG and EOG tests were invariably affected in many retinal disorders and also, progression of the diseases through different layers of the retina could be assessed by using these visual electrophysiological tests [9, 10]. Interestingly our findings of PERG and EOG tests were compatible with the visual electrophysiological findings of typical retinal disorders in other studies as well.

7. Establishment of normal values for PRVEP, PERG and EOG in the Sri Lankan set up

According to the ISCEV guidelines, it is recommended to establish normal values for each laboratory to its own equipment and patient population. There are only a few studies done in the world regarding the normative values of visual electrophysiological tests. In the present study, normal values for the visual electrophysiological measures in a group of healthy adults in Sri Lanka were established. These values can be used in future studies in this regard.

To date, no consensus guidelines have been devised to specify how and when these techniques can be most rationally applied for the diagnostic work-up of patients with various visual disorders in Sri Lanka. Thus, this study series would be an eye-opening series, as the findings arising from these studies could be incorporated to the current guidelines of early diagnosis and screening for different visual disorders in Sri Lankan set up. It should be highlighted that there is a scope for future studies specially on follow up evaluation of the patients with abnormal parameters to determine the prognosis of them and to determine the long-term impact of those disorders on visual electrophysiological parameters. Also, this study finding would help to approach to accomplish the goal of better vision and prevention of blindness in Sri Lanka in the near future.
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Author declaration
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