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Optical coherence tomography parameters in patients with photosensitive juvenile myoclonic epilepsy

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ABSTRACT

Purpose: Juvenile myoclonic epilepsy (JME) is commonly associated with photoparoxysmal response (PPR) with a reported prevalence of 25–42%. In this study, we aim to explore the relationship between the PPR and Optical Coherence Tomography (OCT) parameters in order to determine whether optic nerve fiber layer or other structural differences have a pathophysiological role of photosensitivity in patients with JME.

Methods: We studied 53 consecutive patients with Juvenile myoclonic epilepsy (JME) at our outpatient department. The interictal electroencephalogram (EEG) findings for each patient were analyzed for the presence of photoparoxysmal features. The peripapillary Retina Nerve Fiber Layer (RNFL) thickness, ganglion cell thickness, macular thickness and choroid thickness levels were analyzed using OCT.

Results: We classified the patients into two groups as those with PPR (Group 1) and those without PPR (Group 2). There were statistically significant differences in the average RNFL thickness values of the left eye between the two groups ($p < 0.001$). Although the RNFL thickness of the right eye was higher in Group 1, no statistically significant difference was observed between the two groups. The RFNL thickness of the superior quadrants both in the right and the left eyes was significantly higher in Group 1 patients ($p < 0.001$). Macular thickness of the right and left eyes were significantly thinner in Group 1 patients ($p < 0.001$). Choroid thickness of the left eye was significantly higher in Group 1 than in Group 2 patients ($p < 0.001$). Although the choroid thickness of the right eye was higher in Group 1 patients, no statistically significant difference was observed between the two groups.

Conclusion: This is the first study to our knowledge which has investigated the relation between the OCT parameters and photosensitivity in patients with JME. We concluded that these microstructural features may be related to photosensitivity in patients with JME.

1. Introduction

JME is a hereditary, generalized form of epilepsy and is estimated to account for approximately 10% of all epilepsies, with a range of 4–11% [1]. Seizures have an age-related onset and are characterized by the triad of myoclonic jerks on awakening, generalized tonic–clonic seizures (GTC) and typical absence seizures. Photosensitivity or photoparoxysmal response (PPR) is defined as the presence of an abnormal response to intermittent photic stimulation (IPS) during an EEG [2] and [3]. Different patterns of PPR were determined as ranging from a localized form of occipital spikes (Grade 1) to the generalized spikes-and-waves or polyspike waves (Grade 4) [4–6] (Table 1). The context of photosensitivity and epilepsy reveals diverse clinical situations. Patients may have seizures that are entirely (or predominantly) visually stimulated, which is sometimes described as "pure photosensitive epilepsy" [7]. By way of alternative, the patient may reveal photosensitivity as an EEG response to IPS in the laboratory and the epilepsy may be with or without visually induced seizures [8]. Among the various syndromes, JME is commonly associated with PPR with a reported prevalence of 25–42% [9].

OCT is a non-invasive technique for cross-sectional imaging of the retinal microstructure and it has been used to evaluate retinal

Abbreviations: OCT, optical coherence tomography; RNFL, retina nerve fiber layer; JME, juvenile myoclonic epilepsy; PPR, photoparoxysmal response.

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Table 1
The different patterns of photoparoxysmal response.[a]

Grade	Type of PPR
Grade 1	Spikes within the occipital rhythm
Grade 2	Parieto-occipital spikes with a biphasic slow wave
Grade 3	Parieto-occipital spikes with a biphasic slow wave and spread to the frontal region
Grade 4	Generalized spikes and waves or polyspikes and waves

PPR: photoparoxysmal response.
[a] Refs. [4–6].

disease and structural optic disc damage associated with glaucoma for more than 20 years. OCT has been successfully used in many neurological conditions such as, multiple sclerosis, neuromyelitis optica, Parkinson disease and Alzheimer disease. The main findings of these studies have been damage of retinal ganglion cells which reflect degenerative changes in the brain, therefore the patterns of changes differ in some aspects [10].

Anyanwu and Ehiri have investigated the ocular defects in patients with photosensitive epilepsy using visual-evoked response (VER) [11]. They observed that since luminance variance is the factor that causes seizures in patients with photosensitive epilepsy, it is apparent that the cells in the visual system of such patients may show a negative reaction to the stimuli which have the propensity to alter the functional status of the visual system. Such changes may result in abnormalities in ocular structures and consequently have a negative impact on the clarity of vision. The correlation between the ocular abnormalities and the interpretations of the changes in the characteristics of the VEP signaled the fact that optic-related atrophies, visual defects, optic neuritis, chiasmal compression, nystagmus, migraine headache, cataracts, and amblyopia were dominant in photosensitive epileptic patients at varying degrees. The results of their study have clearly revealed that although ocular defects in photosensitive epilepsy may not be differentially obvious, VEP measurements can be employed in their diagnosis. Major structural changes of the visual system and their relation to photosensitivity in patients with epilepsy has been researched before; however, microstructural changes in the visual system and their relation to photosensitivity have previously not been documented in such patients. Our hypothesis was that the visual system in photosensitive patients with JME could display microstructural changes. For this reason, in our study we aimed at comparing the RNFL thicknesses and the other structural changes of the retina in JME patients with and without photosensitivity.

There are numerous studies suggesting that PPR is related with extreme excitability and reactivity in the visual cortex [12,13]. Moreover, it has been revealed in several studies that during the PPR, functional changes and changes in the blood stream occur in the supplementary motor area (SMA), the perisylvian area and medial temporal areas, besides the occipital cortex [14–16]. Strigaro et al. documented a defective inhibition in the visual system of photosensitive patients with IGE, using a new VEP technique (Faired pulse flash – VEP) [17]. In a recent study, Vollmar et al. demonstrated in patients with JME the alterations of the mesial frontal connectivity with increased structural connectivity between the prefrontal cognitive cortex and the motor cortex [18]. They found out that the increased connectivity between the SMA and the occipital cortex, which was stronger in photosensitive patients, may explain the provocative effect of photic stimulation in order to elicit frontocentral discharges and seizures. The question here is could a structure similar to that of the increased structural connectivity between the occipital cortex and the SMA exist in the retina or in the connection between the retina and the occipital cortex as well? While being distant from providing a satisfactory answer to this question, we believe that the demonstration of the potential microstructural changes in the retina in photosensitive patients with JME might be a starting point.

In this study we aim to explore the relationship between PPR and OCT parameters in order to determine whether RNFL or other microstructural differences have a pathophysiological role in photosensitivity in patients with JME.

2. Methods

We studied 53 consecutive patients with Juvenile myoclonic epilepsy (JME) at our outpatient department. All patients were diagnosed according to the recommendations by the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE) in 2010 with Genetic Generalised Epilepsy (GGE) and were classified as JME, based on the type of seizures, predominant seizure type, age of onset of seizures and EEG characteristics [19].

The EEG evaluation was performed and analyzed at the same institution. The standard placement of 10–20 electrodes was used for the EEG recordings. The standard recording phase lasted 30 min and the hyperventilation phase lasted 4 min. IPS was performed at dim room lighting, an upright position of the patient and by simultaneous video recording. We used the lamp with circular reflector that delivers flashes with an intensity of 0.70 Joule which at 30 cm from the nasion of the patient. IPS was performed with frequencies of 1, 2, 4, 8, 10, 12, 15, 18, 20, 25, 40, 50, and 60 flashes/s, and 0.5 and 70 Hz filters were used. Each frequency was performed with an interval of at least 7 s between each frequency, and each application was continued for 10 s, during which the eye was kept open in the first five seconds and closed in the last five seconds. The interictal EEG findings for each patient were analyzed for the presence of any generalized or occipital photoparoxysmal features.

Each patient underwent a complete ophthalmological examination by the same physician who was uninformed of the EEG findings of the patients. All patients underwent the best-corrected visual acuity testing, slit-lamp biomicroscopy, intraocular pressure measurement, gonioscopy, dilated funduscopic examination and refraction. The peripapillary RNFL thickness, macular thickness and ganglion cell thickness values were analyzed using OCT (Cirrus HD OCT, Carl Zeiss Meditec, Dublin, CA, USA). RNFL measurements were obtained using a circular sweep of a fixed diameter of 3.45 mm around the optic disc. The choroid thickness was analyzed using an EDI-OCT. The exclusion criteria included a best-corrected visual acuity of less than 0.8 logMAR, corneal disease, retinal disease, uveitis, optic neuropathy, glaucoma or orbital disease and previous ophthalmic surgeries. Subjects were also excluded if they presented with a spherical refractive error greater than ±1D or a cylindrical error greater than 1D.

The study was approved by the Ethical Committee of Antalya Education and Research Hospital. Statistical analyses were performed using Pearson Chi-square test and *t*-test (Independent Samples Test) to determine potentially significant differences, and a p value less than 0.05 was considered significant.

3. Results

We classified the 53 patients in our study into two groups as those with generalized/type 4 PPR (Group 1, 43.4%) and those without PPR (Group 2, 56.6%). No patient's EEG demonstrated occipital spikes.

The 23 patients in Group 1 had an age range between 19 and 49 (mean: 28.4), and 18 of them were female (78%). In Group 2, there were 30 patients, of whom 18 were female (60%). The age range of these patients was 12–41 (mean: 25.4). All patients were caucasian. Most of the patients were right-handed. Two patients