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RESEARCH

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# Role of optical coherence tomography as a diagnostic marker for neurodegeneration in epilepsy: a cross-sectional analytical study

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## Abstract

**Background** Progressive neurodegeneration is a common consequence of epilepsy, which has a negative impact on the patient's quality of life. This study aimed to predict neurodegeneration in patients with epilepsy (PwE) through assessment of the retinal nerve fiber layer (RNFL), ganglion cell complex (GCC) thickness, and central macular thickness (CMT) using optical coherence tomography (OCT).

**Results** A cross-sectional study was done on 60 patients with idiopathic epilepsy and 30 healthy volunteers. They were subjected to a full neurological examination, ophthalmological assessment, and OCT for assessment of retinal layers, and cognitive examination using Addenbrooke's scale. PwE had lower cognitive scores, including memory (13.97 ± 2.52), attention (15.95 ± 1.85), language (24.08 ± 1.71), and fluency (6.10 ± 2.05), compared to controls (20.53 ± 3.5), (17.13 ± 1.53), (24.83 ± 0.99), and (8.87 ± 2.39), respectively. There was a significant thinning in average RNFL thickness (84.27 ± 7.66), inferior RNFL thickness (99.33 ± 10.19), average GCC thickness (83.17 ± 9.76), and superior GCC thickness (84.83 ± 7.27) in the epilepsy group compared to controls (105.70 ± 8.73), (104.93 ± 9.75), (101.50 ± 4.84), and (100.53 ± 4.09), respectively. PwE had significantly higher focal macular volume loss (1.17 ± 1.22) versus (0.11 ± 0.21) and a higher insignificant global macular volume loss (1.88 ± 2.32) versus (1.37 ± 0.65) in controls, respectively. Superior GCC thickness was significantly lower in the uncontrolled patients (82.53 ± 6.23) compared to the controlled patients (87.13 ± 7.60), while CMT was significantly lower in the polytherapy group compared to the monotherapy group. There was a significant positive correlation between the age of epilepsy onset and verbal fluency ($r = 0.382$, $p = 0.003$). Epilepsy duration had significant negative correlations with memory ($r = -0.364$, $p = 0.004$), inferior RNFL thickness ($r = -0.324$, $p = 0.012$), perifoveal thickness ($r = -0.353$, $p = 0.006$), and inferior (perifoveal) thickness ($r = -0.365$, $p = 0.004$).

**Conclusion** PwE receiving anti-seizure medications (ASMs) have reduced GCC, RNFL, and CMT and lower cognitive functions compared to controls. OCT may be a useful tool for detection of neurodegeneration in PwE.

**Keywords** Epilepsy, Neurodegeneration, Optical coherence tomography, Retinal nerve fiber layer, Cognitive functions

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## Background

Epilepsy is a chronic worldwide neurological disease affecting around 50 million people around the world [1]. It was recently classified by the International League Against Epilepsy (ILAE) in 2017 according to the etiology into either idiopathic or symptomatic.

The term idiopathic generalized epilepsy (IGE) formerly means of unknown etiology which was replaced by genetic generalized epilepsy (GGE) being the most accurate however, idiopathic epilepsy is also acceptable especially for focal epilepsy [2]. GGE includes four well-established syndromes: childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy and generalized tonic–clonic seizures. All these syndromes are characterized by normal brain magnetic resonance imaging (MRI) and electroencephalogram (EEG) may show background activity and/or inter-ictal generalized epileptiform discharges [3].

Neurodegeneration is defined as any pathological condition that leads to loss of structure or function of the nerve cells. It is the final pathway of many neurological diseases affecting the brain, not only Alzheimer's disease [4]. Similarly, progressive neuronal degeneration is a common consequence of long-term and/or recurrent seizure activity in epilepsy [5]. Neurodegeneration and tauopathy were found to be associated with all types of epilepsy [6]. Not only grey matter, but also widespread white matter involvement has already been demonstrated in epileptogenesis and in seizure-related degeneration [7]. B amyloid and tau are well-known markers of neurodegeneration that can be assessed by a positron emission tomography (PET) scan and cerebrospinal fluid (CSF) analysis. Another marker for neurodegeneration is brain volume loss, especially hippocampus that can be noticed by conventional MRI [8].

Retina and brain are considered to have a common embryonic origin [9]. Retina is formed of three layers: ganglion cells, which are the retinal nerve fiber layer (RNFL) made up of the ganglion cell axons, the ganglion cell layer (GCL) made up of the ganglion cell bodies, and the inner-plexiform layer (IPL) made up of ganglion cell dendrites [10]. Studying the retina, which has anatomical, embryological, and physiological similarities with the brain, may provide insight about neurodegenerative diseases [11]. A significant association was found between RNFL thinning and lower brain volume as assessed by brain MRI [12]. However, it is not commonly used for assessment of brain neurodegeneration.

Recent studies in epilepsy showed that GCC and RNFL thickness in all regions were discovered to be decreased in the epilepsy group compared to healthy controls [13].

The aim of this study is to assess the extent of neurodegeneration in epileptic patients in comparison with control subjects using OCT and to correlate RNFL thinning as a neurodegenerative marker with neurocognitive function in PwE.

## Methods

This is a cross-sectional analytic study done on 60 patients with idiopathic epilepsy selected from the epilepsy outpatient clinic in the period from 2021 to 2022 (group I) and 30 control subjects matched in age and sex (group II). Their ages ranged from 18 to 40 years. Patients with a history of trauma or surgery to the eye or the orbit, systemic diseases such as diabetes mellitus, hypertension, and dyslipidemia, neurological diseases affecting the optic nerve such as multiple sclerosis and neuromyelitis optica, or those affecting cognition as cerebrovascular insults were excluded from the study. Patients who were found to be encephalopathic, those with lesional epilepsy, or those with cognitive impairment were also excluded. In addition to that, patients on benzodiazepines, topiramate, and vigabatrin were excluded.

All participants were subjected to a medical history, a general and neurological examination according to the epilepsy sheet of the epilepsy clinic, and an ophthalmological assessment of each eye. Optical coherence tomography (OCT) was performed by a trained ophthalmologist at Ophthalmic Laser Outpatient Unit for the measurement of ganglion cell complex (GCC), RNFL thickness, including the overall average, peripapillary RNFL (pRNFL), and quadrant RNFL (superior, inferior, temporal, and nasal). It was performed using the Optovue RTVue TM (Optovue Inc., Fremont, CA, USA) optical coherence tomography machine.

Finally, cognitive assessment was done using the Arabic version of Addenbrooke's Cognitive Examination III (ACEIII). It consists of 19 activities that test five cognitive domains: attention, memory, fluency, language, and visuospatial processing. The result of each activity was to give a total score out of 100 (18 points for attention, 26 for memory, 14 for fluency, 26 for language, and 16 for visuospatial processing). A score of 88 and above is considered normal; a score below 83 is abnormal; and a score between 83 and 87 is inconclusive.

In addition, patients were subjected to an awake interictal electroencephalogram (EEG) using the Nihon Kohden 16-channel EEG machine. MRI of the brain using an MRI scanner (Philips, Achieva 1.5T, Netherlands).

Data were coded and entered using the Statistical Package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data were summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using the unpaired *t* test or analysis of variance (ANOVA) with multiple comparisons post hoc test for normally distributed quantitative variables, while the non-parametric Kruskal–Wallis test and Mann–Whitney test were used for non-normally distributed

quantitative variables [14]. For comparing categorical data, a Chi-square test was performed. An exact test was used instead when the expected frequency was less than 5 [15]. Correlations between quantitative variables were done using the Spearman correlation coefficient [16]. *p*-values less than 0.05 were considered statistically significant. The study was approved by the institutional review board.

## Results

Ninety persons were enrolled in this study; 60 were diagnosed with idiopathic epilepsy (Group I) and 30 were matched control subjects (Group II). None of the studied population were diagnosed to have multiple sclerosis, neuromyelitis optica, or cerebrovascular insults after data collection and analysis. The age of the studied population ranged from 20 to 40 years, with a mean of 29. The disease characteristics, types, and number of ASMs are illustrated in Table 1.

Epilepsy had a significant deleterious effect on different cognitive domains, as tested by Addenbrooke's scale. This was obvious in attention, memory, verbal fluency, language, and the total score of the test; however, visuospatial assessment failed to show that (Table 2).

All patients showed normal MRI results while 22 patients (36.7%) had abnormal EEG findings and 38 patients (63.3%) had normal EEG results, as illustrated in Table 3.

Patients with epilepsy also had a significant detrimental effect on some OCT parameters, such as average and inferior RNFL thickness, average and superior GCC thickness, average and temporal perifoveal thickness, and inferior hemisphere perifoveal thickness. There was also significant focal macular volume loss in PwE, as illustrated in Table 4.

Regarding different disease characteristics, foveal thickness was significantly lower in patients with JME, while uncontrolled epilepsy patients had substantially lower superior GCC thickness. Those with abnormal inter-ictal EEG discharge showed notably reduced superior GCC thickness and foveal thickness. Concerning the ASMs, patients on polytherapy had reduced inferior hemisphere (parafoveal) thickness, inferior (parafoveal) thickness, and perifoveal thickness, as shown in Table 5.

Cognitive functions results of patients showed no significant differences between patients with different EEG results.

According to correlation analysis, a significant positive correlation was observed upon comparing some OCT parameters (RNFL inferior, parafoveal thickness) with particular cognitive functions (attention, memory) and

**Table 1** Descriptive results of the patient's group

| Descriptive results | Patient group (Group I) |
|---|---|
| Age (mean ± SD) | 29.42 ± 5.65 |
| Sex of subjects (males) | 28 (46.7%) |
| Age at onset | 13.83 ± 6.46 |
| Duration of epilepsy | 15.58 ± 7.71 |
| Type of epilepsy | |
| Generalized onset epilepsy | 25(41.7%) |
| JME | 18(41.7%) |
| Focal onset epilepsy | 17(41.7%) |
| Uncontrolled patients | 30(50%) |
| Number of fits per month among uncontrolled group | 2.9 ± 3.8 |
| Number of ASMs used by patient | |
| Monotherapy | 14(23.3%) |
| Double therapy | 42 (70%) |
| Triple therapy | 3 (5.0%) |
| Quadritherapy | 1(1.7%) |
| Type of ASM used by patient | |
| Carbamazepine | 16 (26.7%) |
| Phenytoin | 2 (3.3%) |
| Valproic acid | 32 (53.3%) |
| Lamotrigine | 19 (31.7%) |
| Levetiracetam | 40 (66.7%) |
| Oxcarbazepine | 1(1.7%) |
| Abnormal EEG results | 11(36.7%) |
| Compliance to medications | 100% |

*SD* standard deviation, *%* percent, *JME* juvenile myoclonic epilepsy, *ASM* anti-seizure medication, *EEG* electroencephalogram

**Table 2** Results of Addenbrooke's test among the studied groups

| Addenbrooke's test | Patients (Group I) Mean ± SD | Control (Group II) Mean ± SD | *p*-value |
|---|---|---|---|
| Attention | 15.95 ± 1.85 | 17.13 ± 1.53 | 0.002* |
| Memory | 13.97 ± 2.52 | 20.53 ± 3.35 | < 0.001* |
| Fluency | 6.10 ± 2.05 | 8.87 ± 2.39 | < 0.001* |
| Language | 24.08 ± 1.71 | 24.83 ± 0.99 | 0.010* |
| Visuospatial | 14.42 ± 1.44 | 14.53 ± 1.858 | 0.743 |
| Total score | 74.52 ± 5.71 | 85.9 ± 8.08 | < 0.001* |

*SD* standard deviation

* $p < 0.05$ is statistically significant

**Table 3** EEG results in epileptic patients

| EEG results | Results |
|---|---|
| Abnormal EEG discharge | 22 (36.7%) |
| Normal EEG discharge | 38 (63.3%) |

*EEG* electroencephalogram

**Table 4** OCT results among the studied groups

| 3 OCT results | Patients (Group I) Mean ± SD | Control (Group II) Mean ± SD | *p*-value |
|---|---|---|---|
| I-RNFL thickness | | | |
| 1-Average RNFL thickness | 84.27 ± 7.66 | 105.70 ± 8.73 | < 0.001* |
| 2-Superior RNFL thickness | 95.68 ± 80.09 | 105.80 ± 9.06 | 0.493 |
| 3-Inferior RNFL thickness | 99.33 ± 10.19 | 104.93 ± 9.75 | 0.015* |
| II-GCC thickness | | | |
| 1-Average GCC thickness | 83.17 ± 9.76 | 101.50 ± 4.84 | < 0.001* |
| 2-Superior GCC thickness | 84.83 ± 7.27 | 100.53 ± 4.09 | < 0.001* |
| 3-Inferior GCC thickness | 100.75 ± 7.62 | 101.13 ± 4.39 | 0.763 |
| III-Macular volume | | | |
| 1-FLV | 1.17 ± 1.22 | 0.11 ± 0.21 | < 0.001* |
| 2-GLV | 1.88 ± 2.32 | 1.37 ± 0.65 | 0.3 |
| IV-Macula thickness | | | |
| A-Foveal thickness | 246 ± 24.26 | 235.50 ± 25.40 | 0.06 |
| B-Parafoveal sectors thickness | | | |
| 1-Average parafoveal thickness | 310.15 ± 16.59 | 313.70 ± 9.68 | 0.204 |
| 2-Superior Hemisphere parafoveal thickness | 308.88 ± 15.67 | 316.10 ± 9.89 | 0.009* |
| 3-Inferior hemisphere parafoveal thickness | 307.95 ± 15.64 | 313.60 ± 10.89 | 0.08 |
| 4-Temporal parafoveal thickness | 300.27 ± 15.30 | 303.07 ± 8.16 | 0.352 |
| 5-Superior parafoveal thickness | 312.70 ± 15.13 | 319.60 ± 10.72 | 0.028* |
| 6-Nasal parafoveal thickness | 312.70 ± 17.24 | 315.97 ± 10.42 | 0.268 |
| 7-Inferior parafoveal thickness | 310.62 ± 15.61 | 315.00 ± 10.10 | 0.112 |
| c-Perifoveal sectors thickness | | | |
| 1- Average perifoveal thickness | 257.63 ± 14.73 | 274.73 ± 11.90 | < 0.001* |
| 2- Superior hemisphere perifoveal thickness | 283.50 ± 12.60 | 280.23 ± 13.23 | 0.257 |
| 3-Inferior hemisphere perifoveal thickness | 252.18 ± 14.28 | 271.67 ± 11.96 | < 0.001* |
| 4-Temporal perifoveal thickness | 247.27 ± 13.60 | 257.17 ± 9.12 | < 0.001* |
| 5-Superior perifoveal thickness | 281.85 ± 12.53 | 276.13 ± 10.77 | 0.801 |
| 6-Nasal perifoveal thickness | 294.88 ± 22.35 | 296.13 ± 13.20 | 0.778 |
| 7-Inferior perifoveal thickness | 252.48 ± 12.15 | 268.17 ± 14.13 | < 0.001* |

*OCT* optical coherence tomography, *SD* standard deviation, *RNFL* retinal nerve fiber layer, *GCC* ganglion cell complex, *FLV* focal loss of volume, *GLV* global loss of volume

* $p < 0.05$ is statistically significant

the age of disease onset, denoting the strong relationship between cognitive decline, aging, and associated neurodegeneration.

The age of disease onset also showed a significant positive correlation with perifoveal thickness, inferior (perifoveal) thickness, and verbal fluency.

The current study also showed a significant positive correlation between the thickness of different retinal layers and some cognitive functions. Adding to that, the lower memory scores were associated with increased global retinal volume loss and longer epilepsy duration.

A significant negative correlation was found between some OCT parameters and the duration of epilepsy, as well as the number of ASMs.

A significant positive correlation was found between having a normal EEG result and foveal thickness.

Correlations are illustrated in Table 6.

## Discussion

Progressive neuronal degeneration is a well-known consequence of long-term and/or recurrent seizure activity in epilepsy [5]. Such neurodegeneration can be assessed clinically by cognitive testing or by investigational methods such as brain volume loss or, rather, an indirect method in the form of retinal thickness assessment, which is structurally linked to the brain [9].

The current study showed that epilepsy had a significant negative effect on cognitive functions. It affects

**Table 5** OCT findings in different epileptic patients

| OCT results | Disease characteristics | | *p*-value |
|---|---|---|---|
| | **Type of epilepsy** | | |
| | **Juvenile myoclonic epilepsy** | **Other generalized-onset epilepsies** | |
| Foveal thickness | 231.39 ± 19.29 | 246.35 ± 18.76 | 0.002* |
| | **Controlled or uncontrolled epilepsy** | | |
| | **Uncontrolled** | **Controlled** | |
| Superior GCC thickness | 82.53 ± 6.23 | 87.13 ± 7.60 | 0.013* |
| | **Inter-ictal EEG findings** | | |
| | **Abnormal EEG** | **Normal EEG** | |
| Superior GCC thickness | 82.23 ± 6.45 | 86.34 ± 7.37 | 0.033* |
| Foveal thickness | 239.79 ± 23.05 | 256.73 ± 22.96 | 0.008* |
| | **Monotherapy versus polytherapy** | | |
| | **Monotherapy** | **Polytherapy** | |
| Inferior hemisphere (parafoveal) | 310.13 ± 15.46 | 300.79 ± 14.53 | 0.049* |
| Inferior (parafoveal) thickness | 313.39 ± 14.72 | 301.50 ± 15.45 | 0.011* |
| Perifoveal thickness | 259.85 ± 15.57 | 250.36 ± 8.45 | 0.034* |

*OCT* optical coherence tomography, *GCC* ganglion cell complex, *EEG* electroencephalogram

* $p < 0.05$ is statistically significant

**Table 6** Correlations

| | Age of onset | | Duration of epilepsy | | Number of ASMs | | Attention | | Memory | | Visuospatial | | EEG | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* | *r* | *p* |
| RNFL inferior | 0.270 | 0.037* | − 0.324 | 0.012* | | | 0.282 | 0.029* | 0.338 | 0.008* | | | | |
| Foveal thickness | | | | | | | | | | | | | 0.322 | 0.012 |
| RNFL superior | | | | | | | 0.279 | 0.031* | 0.330 | 0.01* | 0.265 | 0.041* | | |
| Parafoveal thickness | 0.257 | 0.048* | | | | | 0.257 | 0.048 | 0.315 | 0.014* | | | | |
| Perifoveal thickness | 0.309 | 0.016* | − 0.353 | 0.006* | | | 0.102 | 0.436 | 0.278 | 0.032* | | | | |
| Inferior (perifoveal) thickness | 0.444 | 0.000* | − 0.365 | 0.004* | | | 0.251 | 0.053 | 0.306 | 0.018* | | | | |
| Inferior (parafoveal) Thickness | | | | | − 0.279 | 0.031* | | | | | | | | |
| Inferior GCC thickness | | | | | | | 0.204 | 0.118 | 0.350 | 0.006* | | | | |
| GLV | | | | | | | − 0.086 | 0.516 | − 0.334 | 0.009* | | | | |
| Duration of epilepsy | | | | | | | | | − 0.364 | 0.004* | | | | |
| Verbal fluency | 0.382 | 0.003 | | | | | | | | | | | | |

*ASMs* anti-seizure medications, *EEG* electroencephalogram, *r* Spearman correlation coefficient, *RNFL* retinal nerve fiber layer, *GCC* ganglion cell complex, *GLV* global loss of volume

* $p < 0.05$ is statistically significant

attention, memory, language, and fluency, which was consistent with many previous studies [17–20].

However, Wang and his colleagues found no association between epilepsy and cognitive functions, especially verbal fluency, which may be attributed to different patients' characteristics and different assessment measures [21].

Disruption of the neuronal activity that is seen as a part of seizures, post-ictal derangement, and inter-ictal epileptic discharges that occur especially during sleep

leads to progressive loss of neuronal function, death of cells, and subsequently cognitive decline [22].

The current work states that epilepsy has a noxious effect on different retinal layers. It resulted in a significant thinning of the average overall RNFL thickness and the different quadrants, especially the superior and inferior, as shown by de la Aleja and his colleagues and also by Bayraktar Bilen and his colleagues [13, 23].

Significant thinning of the average overall GCC thickness and the different quadrants, especially the superior one, was also noted [13].

In the present work, a significant focal macular volume loss as well as thinning in the different macular areas, especially superior parafoveal, superior hemisphere parafoveal, average perifoveal, inferior perifoveal thickness, inferior hemisphere perifoveal, and temporal perifoveal, are seen in PwE, which agrees with Gomceli and his colleagues [24]. However, de la Aleja and his colleagues found no associations between thinning of different retinal layers (RNFL, GCC, macula) and epilepsy, which may be attributed to the low number of enrolled patients as well as different patients' characteristics [23].

According to the type of epilepsy, patients with JME showed significantly greater foveal thinning than other generalized-onset epilepsies, which agrees with Gomceli and his colleagues who enrolled patients with photoparoxysmal response (PPR) [24]. Despite the fact that in our study we did not classify our patients according to photosensitivity, we rely on the commonly associated photosensitivity with JME to indicate the existence of microstructural retinal changes as detected by OCT. While this finding disagrees with Balestrini and his colleagues, it may be related to different assessment methods [12].

It also showed a significant thinning of superior GCC in uncontrolled patients, which agrees with Balestrini and his colleagues [12]. This may be due to further cerebral damage caused by continuous ongoing seizures that may manifest in a lowering of the brain parenchymal fraction and is seen in the form of thinning of the RNFL.

The current work revealed a significant macular thinning in PwE on polytherapy, especially in the perifoveal, inferior parafoveal, and inferior hemisphere parafoveal. Bayraktar and his colleagues agreed with these results [13]. This is because most of the patients on polytherapy have drug-resistant epilepsy, so there is continuous epileptic firing that leads to brain neurodegeneration, as mentioned earlier. Adding to that, the etiology of epilepsy and the toxic consequences of the long-term use of ASMs may play a role.

However, Tak and his colleagues, who assessed only the RNFL and GCC and not the macular layers, did not find any association between multiple drug use and OCT parameters [10].

In this study, the older the age of epilepsy onset, the significantly better the verbal fluency as well as OCT parameters, especially inferior RNFL, parafoveal, perifoveal, and inferior (perifoveal) thickness. This goes in agreement with Kim and his colleagues and Chawla and his colleagues indicating that the early onset of epilepsy affects brain plasticity and integrity, which may be reflected in cognitive abilities such as fluency. However, the occurrence of retrograde trans-synaptic degeneration may result in the loss of fibers at the optic nerve head (ONH) and macula [19, 25].

A negative correlation between the duration of epilepsy and memory was found, which agreed with Wang and his colleagues, who attributed that to cumulative neuronal damage occurring gradually as a result of the disease leading to abnormal cerebral morphological and metabolic changes [21]. However, Arida and his colleagues found no correlation between the disease and memory as they enrolled patients with temporal lobe epilepsy, pointed to the existence of cognitive affection as early as disease began, and described that cognitive decline may be a waterfall rather than a gradual process [26].

The duration of epilepsy as well was inversely proportionate to some OCT parameters (inferior RNFL thickness, perifoveal thickness, inferior perifoveal thickness) in a significant manner, which agrees with Bayraktar and his colleagues [13]. He attributed that to progressive neuronal damage that leads to RNFL and macular thinning. However, Xiong and his colleagues found no significant correlation between the duration of epilepsy and RNFL, which may be attributed to a different study population [27].

The current study revealed a significant negative correlation between the number of ASMs and inferior (parafoveal) thickness, which reflects that the more difficult it is to control the disease process, the more neuronal degeneration occurs.

To the best of our knowledge, no previous studies in the literature support the following findings: we found for the first time that RNFL and macular OCT parameter values predict subsequent cognitive decline in patients with epilepsy. This is because this work shows a significant positive correlation between cognitive functions and some of the OCT parameters.

In the illustration of what was mentioned formerly, the following were detected: a positive significant correlation between attention and the following parameters (superior RNFL thickness, inferior RNFL, parafoveal thickness), a positive significant correlation between memory and the following parameters (inferior GCC, superior RNFL, inferior RNFL, parafoveal,

perifoveal, inferior perifoveal thickness), a significant positive correlation between visuospatial and superior RNFL thickness, and finally a significant negative correlation between memory and GLV.

## Conclusion

From the current study, we could conclude that OCT parameters (ganglion cell complex, retinal nerve fiber layer thickness, and central macular thickness) were notably reduced in PwE, reflecting generalized neurodegeneration manifested clinically by impairment of important cognitive parameters such as attention, memory, and visuospatial.

There were some limitations in this study. First, this study is a single-center observational study done on a small number of patients. A long-term study with a large number of patients is required for further comments. Second, the study was conducted at a university hospital, which is a tertiary hospital and may include more severe and complicated cases. Finally, this study was done during the Corona virus disease 2019 (COVID-19) era, in which many patients preferred not to seek medical advice unless there had been a catastrophe.

### Abbreviations

| | |
|---|---|
| PwE | Patients with epilepsy |
| RNFL | Retinal nerve fiber layer |
| GCC | Ganglion cell complex |
| CMT | Central macular thickness |
| OCT | Optical coherence tomography |
| ASMs | Anti-seizure medications |
| GCL | Ganglion cell layer |
| ILAE | The International League Against Epilepsy |
| IGE | Idiopathic generalized epilepsy |
| GGE | Genetic generalized epilepsy |
| MRI | Magnetic resonance imaging |
| EEG | Electroencephalogram |
| PET | Positron emission tomography |
| CSF | Cerebrospinal fluid |
| IPL | Inner-plexiform layer |
| ACEIII | Addenbrooke's Cognitive Examination III |
| SPSS | Statistical Package for the Social Sciences |
| JME | Juvenile myoclonic epilepsy |
| FLV | Focal loss of volume |
| GLV | Global loss of volume |
| PPR | Photoparoxysmal response |
| ONH | Optic nerve head |

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### Author contributions

AMR conceptualized the study and shared in data collection and the supervision of all the steps. MH shared in data collection and supervision. EE shared in data collection and supervision. MS shared in data collection and supervision. HM shared in data collections, data analysis and interpretation. DAM and HM wrote the manuscript. HM is the submitting and corresponding author. The final version has been read, revised, and edited by all authors to be submitted for publication.

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

The study protocol was approved by the Medical Research Ethics Committee at Kasr Al Ainy School of Medicine, Cairo University, Cairo, Egypt, under number (MD-105-2021). Written informed consent was obtained from all participants.

### Consent for publication

The consents of publication are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.

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