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Assessment of severity of Parkinson's disease by optical coherence tomography

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ABSTRACT

Background: Parkinson's disease (PD) is the second most common movement disorder after essential tremor. Diminished visual acuity, color vision, and contrast sensitivity are also described in PD. Optical coherence tomography (OCT), a producible test for axonal degeneration, helps in prognosticating diseases such as Alzheimer's, Parkinson's, and multiple sclerosis. **Aims and Objectives:** To assess the severity of Parkinson's disease with the changes in various variables of OCT. The objective is to evaluate variables such as (RNFL, CMT, TMV) of both eyes with SD – OCT. **Materials and Methods:** It is a hospital-based cross-sectional study conducted for a period of 22 months at the department of neurology. A total of 55 PD patients and 30 age- and sex-matched controls were evaluated. **Results:** There was a significant difference between patients and controls in average retinal nerve fiber layer (RNFL) and all RNFL quadrants in both the eyes ($P<0.001$). A significant negative correlation was found between the RNFL thickness and Unified Parkinson's Disease Rating Scale (UPDRS) motor score and Hoehn and Yahr (H&Y) score in both the eyes ($P<0.001$). A significant negative correlation was found between total macular volume (TMV) and central macular thickness (CMT) with UPDRS motor score in both the eyes ($P<0.001$). A significant negative correlation was found between CMT and H&Y stage in both the eyes ($P<0.001$). There was a significant difference between patients and controls in CMT and TMV in both the eyes ($P<0.001$). **Conclusion:** A significant negative correlation between severity and stage of the PD with OCT values was identified, which may suggest the possibility of dopaminergic depletion in the retina corresponding with basal ganglia dopamine depletion.

Key words: Optical coherence tomography; Parkinson's disease; Retinal nerve fiber layer

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INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor and non-motor phenomenon. The motor phenomenon being resting tremor, rigidity, bradykinesia and postural instability.[1] The non-motor symptoms are mood disorders, sleep disturbances, Orthostatic hypotension, loss of smell, cognitive decline and visual impairment.[2]

The severity of motor symptoms can be used as an independent predictor of mortality in patients with PD.[3] It has an estimated incidence of8–18/100,000 person-years with a prevalence of 0.3% (De Lau and Breteler, 2006).[4]

Diminished visual acuity, color vision, and contrast sensitivity are some of the visual disturbances described in PD.[5-7] Dopamine dysfunction in PD is seen not only in the basal ganglia but also in retina, especially in the horizontal, amacrine, bipolar, and ganglion cells.[8] Data suggest that several neurologic conditions have pathologic changes in the retinal nerve fiber layer (RNFL) of the eye, creating a potential surrogate marker for neurodegeneration. In an autopsy study of eight patients, Harnois et al., found that the dopamine content of retina is decreased in PD.[9]

Optical coherence tomography (OCT) is a relatively new non-invasive, non-contact transpupillary imaging

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technology. It provides high-resolution, cross-sectional images of the retina. It measures anatomic layers of the retina with an axial resolution of ≤10 ff and a transverse resolution of 20 μm in the eye. It is a producible test for axonal degeneration that could measure alterations in the rate of degeneration and helps in prognosticating the diseases such as Alzheimer's, Parkinson's, and multiple sclerosis when treatment applied.

In recent years, OCT provides direct *in vivo* visualization of retinal structure and retinopathy in PD. Recent histopathological studies confirmed the involvement of the retina in PD by describing the presence of alpha-synuclein deposition in the inner retina.[10,11] Thus, OCT represents a new promising technology for documenting outcomes in PD.

Aims and objectives

Aim: To assess the severity of Parkinson's disease with the changes in various variables of OCT.

Objective: To evaluate the Retinal Nerve Fibre Layer Thickness (RNFL), Central Macular Thickness (CMT) & Total Macular Volume (TMV) of both eyes with SD – OCT in Parkinson's disease and hence exploring the utility of OCT.

MATERIALS AND METHODS

It is a hospital-based cross-sectional study conducted for a period of 22 months (January 2016–November 2017) at the Department of Neurology, Vydehi Institute of Medical Sciences and Research Centre (VIMS and RC), Bengaluru, on obtaining the approval from Vydehi Institutional Ethics Committee. Seventy patients with clinical features of PD were enrolled into the study. Out of them, 55 patients who fulfilled the inclusion and exclusion criteria were enrolled. Thirty age- and sex-matched controls were included in the study.

Neurological evaluation

Detailed clinical history and examination with UK Parkinson's Disease Society Brain Bank Clinical Diagnostic criteria, Hoehn and Yahr (H&Y) stage assessment, and motor assessment using the part III of the Unified Parkinson's Disease Rating Scale (UPDRS motor score) were used.

Ophthalmic evaluation

All the study patients underwent complete ophthalmic evaluation. It included:

1. Visual acuity was determined using Snellen chart, measurement of intraocular pressure (IOP) using the tonometer, and detailed fundus examination (direct and indirect).
2. IOP was assessed using Goldmann applanation tonometry.
3. Goldmann single mirror gonioscope was used to assess the anterior chamber angle to rule out narrow angle glaucoma.
4. Using the SD-OCT, that is, Cirrus OCT, Carl Zeiss Meditec, India., the retinal and optic nerve head imaging was done to study the RNFL thickness of four quadrants – inferior, superior, nasal, and temporal, along with its average thickness. Furthermore, the central macular thickness (CMT) and total macular volume (TMV) were studied. The CMT was defined as the distance between the inner limiting membrane to the outer border of the retinal pigment epithelium through the automatic segmentation algorithms of the Stratus OCT Review software Version 5.0.1 (0376) software. The high acquisition speed of the instrument (27,000 axial sections per second) was used to avoid the artifacts from the microsaccades and thus the image definition will be of good quality.
5. The RNFL thickness (from the inner margin of the internal limiting membrane to the outer margin of the RNFL layer) was automatically segmented using the Stratus OCT software version. SD-OCT shows the results of macular thickness measurements in circles of 1 mm, 3 mm, and 6 mm. The average retinal thickness at the fovea centered around 500 mm of the macula was taken as the CMT, the average retinal volume in the 6 mm circle as the TMV.

On obtaining informed consent, study subjects were evaluated for both neurological and ophthalmic evaluations.

Inclusion criteria

Patients diagnosed with idiopathic PD based on UK Parkinson's Disease Society Brain Bank Clinical Diagnostic criteria attending the neurology OPD at VIMS and RC. Thirty age- and sex-matched controls were included in the study.

Exclusion criteria

Patients with atypical and secondary Parkinsonism syndromes/other neurodegenerative disorders, glaucoma, retinal diseases (local/systemic illnesses) with a history of ocular surgery, and laser therapy to eye were excluded from the study.

RESULTS

The mean age of the PD patients was 59.45±7.22 years with a range of 45–75 years and that of the control group was 55.80±8.47 years with the range being 42–72 years. The majority of the patients were in the 5th decade followed by

the 6th decade (50.9% and 30.9%, respectively) which was statistically significant (P=0.039). The majority were male (56.4%) in our study which was consistent with most of the studies.

The mean duration of PD illness in our study was 3.43±2.96 years (range 0.5–15 years). The majority of the patients (80%) were in early years of their illness. Almost 70.9% were not suffering with any comorbidities, 29.1% suffering with comorbidities in which majority had systemic hypertension (18.2%) followed by Type-2 diabetes mellitus (5.1%).

In our study, 96% of the case cohorts were in normal Mini-Mental State Examination (MMSE) range and have showed the Mean±SD: 27.53±1.61 (Table 1).

The mean UPDRS motor score of PD patients in our study was 17.89±9.57 with a range of 7–46 (Table 2).

The mean H&Y score stage of PD patients in our study was 2.0±0.57 with a range 1–3 (Table 3).

The RNFL thickness of the 55 patients was compared with that of age and gender matched 30 controls. There was a significant difference between the patients and controls in average RNFL and all RNFL quadrants in both the eyes (Tables 4 and 5). There was a significant difference between the patients and controls in TMV in both the eyes (patient's: Mean value = 9.2±1.13 and 9.13±1.1 right and left, respectively, Control's: Mean value = 7.28±0.3 and 7.32±0.31 right and left, respectively) (Table 4 and 5).

Table 1: Mini-Mental State Examination distribution

MMSE	No.of patients	Percentage
25–30	53	96.4
20–25	1	1.8
10–20	1	1.8
<10	0	0.0
Total	55	100.0

MMSE: Mini-Mental State Examination

Table 2: UPDRS (motor score) distribution

UPDRS motor score	No.of patients	Mean
<10	7	12.7
10–30	42	76.4
>30	6	10.9
Total	55	100.0

UPDRS: Unified Parkinson's Disease Rating Scale

Table 3: H&Y score stage distribution

H&Y stage	No.of patients	Mean
1	9	16.4
1.5	2	3.6
2	30	54.5
2.5	8	14.5
3	6	10.9
Total	55	100.0

H&Y: Hoehn and Yahr

The CMT of 55 patients was compared with that of age- and gender-matched 30 controls. There was a significant difference between patients and controls in CMT in both the eyes (patient's mean value = 221.25±9.5 and 222.09±8.71 right and left, respectively, control's mean value = 242.47±5.59 and 243.13±5.69) (Tables 4 and 5).

A significant negative correlation was found between RNFL thickness and UPDRS motor score in both the eyes (P<0.05) (Table 6). In the right eye, significance is seen in the order of inferior> temporal> superior quadrants(r=−0.812, −0.695, and −0.693, respectively) with moderate correlation between RNFL nasal quadrant and UPDRS motor score (r=−0.39). In the left eye, significance is in the order of inferior>nasal>temporal quadrants (r=−0.749, −0.451, and −0.440, respectively) with moderate correlation between RNFL superior quadrant and UPDRS motor score (r=−0.34).

A significant negative correlation was found between TMV and UPDRS motor score in both the eyes i.e in the right eye, r=−0.738, P<0.001 and left r=0.717, P<0.001. A significant negative correlation was found between CMT and UPDRS motor score in both the eyes

i.e in the right eye, r=−0.798, P<0.001and left r=0.807, P<0.001.

No correlation was found between RNFL thickness and age of the patients, MMSE, or duration of disease except for the duration of illness versus RNFL inferior quadrant with P=0.045 (Table 7).

A significant negative correlation was found between the RNFL thickness and the H&Y score in both the eyes (P<0.05). In the right eye, significance was seen in the order of temporal>superior>inferior>nasal (r = −0.696, −0.654, −0.625, and −0.533, respectively) whereas in the left eye, significance seen in the order of inferior>nasal>temporal>superior quadrants (r = −0.630, −0.539, −0.452, and −0.424, respectively).

A significant negative correlation was found between the TMV and the H&Y stage in both the eyes i.e in the right eye, the r=−0.483;P<0.001and on the left r=−0.521; P<0.001.

A significant negative correlation was found between the CMT and H&Y stage in both the eyes i.e in the

Table 4: OCT variables studied in the right eye

OCT variables	Cases	Controls	Total	P value
RNFL average	76.63±8.98	94.55±4.55	82.96±11.54	<0.001**
RNFL inferior quadrant	90.76±17.39	119.10±8.70	100.76±20.15	<0.001**
RNFL superior quadrant	100.90±11.57	118.53±6.26	107.12±13.09	<0.001**
RNFL nasal quadrant	65.42±9.24	70.53±4.49	67.23±8.24	<0.001**
RNFL temporal quadrant	49.19±7.03	69.60±3.38	56.39±11.49	<0.001**
Total macular volume	9.20±1.13	7.28±0.30	8.52±1.31	<0.001**
Central macular thickness	221.25±9.50	242.47±5.59	228.74±13.14	<0.001**

Applied Student's t-test (P<0.001). OCT: Optical coherence tomography, RNFL: Retinal nerve fiber layer, ** Represents – Statistically highly significant

Table 5: OCT variables studied in the left eye

OCT variables	Cases	Controls	Total	P value
RNFL average	78.00±7.52	95.59±4.62	84.21±10.73	<0.001**
RNFL inferior quadrant	93.01±13.25	120.4±7.41	102.68±17.47	<0.001**
RNFL superior quadrant	102.77±10.91	119.87±7.04	108.8±12.70	<0.001**
RNFL nasal quadrant	65.02±8.29	71.07±4.85	67.15±7.80	<0.001**
RNFL temporal quadrant	51.17±7.82	71.03±3.88	58.18±11.65	<0.001**
Total macular volume	9.13±1.10	7.32±0.31	8.49±1.26	<0.001**
Central macular thickness	222.09±8.71	243.13±5.69	229.52±12.74	<0.001**

Applied Student'st-test (P<0.001). OCT: Optical coherence tomography, RNFL: Retinal nerve fiber layer, ** Represents – Statistically highly significant

Table 6: Pearson correlation of UPDRS3 with OCT variables

UPDRS3 versus OCT variables	Right eye		Left eye	
	r value	P value	r value	P value
UPDRS3 versus RNFL average	−0.866	<0.001**	−0.693	<0.001**
UPDRS3 versus RNFL inferior quadrant	−0.812	<0.001**	−0.749	<0.001**
UPDRS3 versus RNFL superior quadrant	−0.693	<0.001**	−0.343	0.010**
UPDRS3 versus RNFL nasal quadrant	−0.392	0.003**	−0.451	0.001**
UPDRS3 versus RNFL temporal quadrant	−0.695	<0.001**	−0.440	0.001**
UPDRS3 versus total macular volume	−0.738	<0.001**	−0.717	<0.001**
UPDRS3 versus central macular thickness	−0.798	<0.001**	−0.807	<0.001**

"r" value represents Pearson correlationcoefficient, P value – represents probability. OCT: Optical coherence tomography, RNFL: Retinal nerve fiber layer, UPDRS: Unified Parkinson's Disease Rating Scale, ** Represents – Statistically highly significant

Table 7: Pearson correlation of duration of illness with OCT variables in the right eye and left eye

Duration of illness versus OCT variables	Righteye		Lefteye	
	r value	P value	r value	P value
Duration of illness versus RNFL average	−0.210	0.127	−0.174	0.208
Duration of illness versus RNFL inferior quadrant	−0.217	0.115	−0.274	0.045*
Duration of illness versus RNFL superior quadrant	−0.096	0.489	−0.074	0.595
Duration of illness versus RNFL nasal quadrant	−0.167	0.226	−0.062	0.656
Duration of illness versus RNFL temporal quadrant	−0.165	0.232	−0.099	0.478
Duration of illness versus total macular volume	−0.131	0.346	−0.051	0.712
Duration of illness versus central macular thickness	−0.123	0.375	−0.108	0.438

"r" value represents Pearson correlation coefficient. OCT: Optical coherence tomography, RNFL: Retinal nerve fiber layer, * Represents – Statistically significant

right eye, r=−0.714;P<0.001and on the left r=−0.650; P<0.001(Table 8).

DISCUSSION

The mean age of the patient group in our study (Mean±SD: 59.45±7.22 years) was correlating with most of the studies done by Inzelberg et al.,[12] Altintaş et al.,[13] Moschos et al.,[14] and Kirbas et al.,[15] who compared the PD and OCT values.

The results of our study showed a significant negative correlation of RNFL, TMV, and CMT with UPDRS motor scores and H&Y stages. The thickness of RNFL of patients with PD was significantly different from that of controls in all quadrants. In addition, a significant

Table 8: Pearson correlationof H&Y stage with OCT variables in the right eye and left eye

H&Y stage versus OCT variables	Right eye		Left eye	
	r value	P value	r value	P value
H&Y stage versus RNFL average	−0.818	<0.001**	−0.695	<0.001**
H&Y stage versus RNFL inferior quadrant	−0.625	<0.001**	−0.630	<0.001**
H &Y stage versus RNFL superior quadrant	−0.654	<0.001**	−0.424	<0.001**
H&Y stage versus RNFL nasal quadrant	−0.553	<0.001**	−0.539	<0.001**
H&Y stage versus RNFL temporal quadrant	−0.696	<0.001**	−0.452	0.001**
H&Y stage versus total macular volume	−0.483	<0.001**	−0.521	<0.001**
H&Y stage versus central macular thickness	−0.714	<0.001**	−0.650	<0.001**

H&Y: Hoehn and Yahr, OCT: Optical coherence tomography, RFNL: Retinal nerve fiber layer, ** Represents – Statistically highly significant

decrease in CMT and increase in TMV was noted in patients with PD.

RNFL

A recent study by Satue et al.,[16] with a large sample size of 100 patients and 100 healthy controls reported decreased thickness of RNFL in supra- and inferotemporal quadrant. However, the mean age of the patients was higher (64 years vs. 59 years) compared to that of patients in our study.

A study done by Rohani et al.,[17] (N: PD=27, C=25) showed that the RNFL thickness in all four quadrants was lower in patients with PD compared to controls. Furthermore, in their study, they compared the RNFL thickness between two subgroups (akinetic dominant and tremor dominant) of PD and found that inferior and nasal quadrants were thinner in akinetic rigid subgroup. Comparison of RNFL thickness between the different subgroups could not be attempted in our study as majority of our patients had tremor dominant subtype of PD (only eight were akinetic dominant of the total 55 PD patients).

There was a significant negative correlation found between RNFL thickness and UPDRS motor score and H&Y stage in the present study. The maximum significance is noted in the inferior quadrant along with the RNFL average also being significant. A study done by Mailankondy et al., (N: PD=27, C=25) in the same ethnic population as our study, showed negative correlation of RNFL with the disease severity with both UPDRS and H & Y stages, which was similar to our study. A negative correlation of RNFL with the disease severity was found by Garcia-Martin et al., (N: PD=46, C=33) and Jiménez et al. However, Garcia-Martin et al.,[18] correlated RNFL with only H&Y stage and Jiménez et al.,[19] only with UPDRS scores.

A lower mean duration of disease (3.43±2.9 years) as compared to other studies might have contributed to lack of significant difference between duration of illness and RNFL variables in our study.

In our study, we found that there is a strongly significant difference in the RNFL thickness of all four quadrants and average thickness, between the patient and control cohorts. The results were conflicting in different studies which measured RNFL thickness in PD patients. Most of the studies have shown decreased thickness of RNFL in PD when compared to controls. On the contrary to our study, several studies have reported RNFL thickness to be similar in patients and controls.[20,21]

A study done by Jiménez et al., (N: PD=52,C=50) showed that the RNFL thickness in all four quadrants was lower in patients with PD compared to controls. Furthermore, a strong inverse correlation was found between PD severity measured according to the UPDRS score and the average RNFL thickness ($r=-0.615$; $P<0.001$) and PD duration ($r=-0.303$; $P=0.002$). However, we could not get any correlation with the RNFL values and duration of the disease with $P>0.05$.

This suggests the possibility of dopaminergic depletion in the retina concurrent with that of the basal ganglia or another unknown mechanism associated to pathophysiological process of PD that needs further elucidation and workup in the future studies.

CMT

CMT was found to be significantly reduced on both the sides in patients with PD as compared to the age- and gender-matched controls in our study and there was no asymmetry between the sides. Several other studies done by Mailankondy et al., Satue et al., and Garcia-Martin et al., have also found that there is a decreased CMT in cohorts with PD compared to controls.

In contrary to this observation, studies done by Altintaş et al., Aaker et al., Archibald et al., Albrecht et al.,[22] and Shrier et al.,[23] did not show any significance in the CMT values between PD and control cohorts. Furthermore, Shrier et al., (N: PD=23, C=18) found that there was asymmetry between the CMT of two eyes in contrary to our study group where the symmetry was maintained between the two sides.

In our study, we found a significant negative correlation between CMT and PD severity scores both UPDRS and H&Y stages in both the eyes. Similarly, Altintaş et al. found a significant negative correlation between CMT and UPDRS motor scores. The study done by Mailankondy et al., showed that the there is a significant negative correlation on the right with the UPDRS scores, unlike our study which showed the negative correlation in both the eyes.

Since the fovea predominantly consists of cones which receive direct input from the dopaminergic cells,[24] the thinning of the CMT reflects dopaminergic depletion in the fovea. The negative correlation with the severity of the disease further supports the notion of dopaminergic depletion.

TMV

In our study, the TMV was significantly greater (9.20±1.13 mm^3 and 9.13±1.10 mm^3; right and left eyes, respectively) in PD patients as compared to the controls. There is a symmetry of TMV between the two eyes. The study done by Mailankondy et al., also showed that there is a significantly greater TMV in both the eyes.

On the contrary, Altintaş et al., and Shrier et al., reported a significantly lower mean TMV in patients compared to controls. The reason for this could be the mean age and duration of PD is much more higher compared to our group who had a lower mean duration of illness (Mean±SD: 3.43±2.96 years). Archibald et al., have found that the macular volumes were not significant between the patients and controls.

In our study, we found a significant negative correlation between the TMV and PD severity scores of both UPDRS 3 and H&Y stages in both the eyes. To the best of our knowledge, this is the first study which has evaluated the correlation with the severity of PD and the TMV values.

The reason for a higher TMV in the presence of thinner fovea in our patients is not clear. It is possible that cell swelling seen in the early stage of cell death[25] of retinal ganglion cells may contribute to the increased macular volume seen on OCT in our group. In relation to this statement, we found patients with UPDRS motor score of >40 (n=3), the TMV in both the eyes was <6 mm^3 which was low in comparison to controls. A follow-up study may detect a gradual reduction in the macular volume of the present patients which eventually presents with ganglion cell loss and therefore thinned out RNFL.

Limitations of our study

The present study was a cross-sectional type. The study population included in our study is heterogeneous with respect to:

1. Duration of disease (0.5–15 years),
2. Stage of the disease (H&Y: 1–3) and
3. Severity of UPDRS motors cores: 7–46.

A contradictory finding of decrease in CMT with an increase in TMV was probably due to the fact that patients were in different stages of the disease. We were unable to ascertain the temporal relationship between OCT and drug intake and drug response.

These things call for a longitudinal follow-up study, which may include larger PD population having similar stages and severity scores and hence be useful in ascertaining the changes that occur with each time in the macular volumes, thickness, and RNFL.

CONCLUSION

To the best of our knowledge, this is one of the first studies which included large group of PD cohorts in South East Asian population, analyzing the changes in the retina using the SD-OCT and comparing with the severity of PD. Our study demonstrated a statistically significant difference in the OCT values in study subjects. There was a significant negative correlation between the severity and stage of the PD illness with the OCT variables studied. These findings suggest the possibility of dopaminergic depletion in the retina. A further long-term follow-up study may be useful in assessing and demonstrating the progressive decrease in TMV over time and OCT as a diagnostic marker for PD management and prognostication.

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REFERENCES

1. Jankovic J. Parkinson's disease: Clinical features and diagnosis. J Neurol Neurosurg Psychiatry. 2008;79(4):368-376. https://doi.org/10.1136/jnnp.2007.131045
2. Chaudhuri KR, Healy DG, Schapira AH and National Institute for Clinical Excellence. Non-motor symptoms of Parkinson's disease: Diagnosis and management. Lancet Neurol. 2006;5(3):235-245. https://doi.org/10.1016/S1474-4422(06)70373-8
3. Forsaa EB, Larsen JP, Wentzel-Larsen T and Alves G. What predicts mortality in Parkinson disease? A prospective population-based long-term study. Neurology. 2010;75(14):1270-1276. https://doi.org/10.1212/WNL.0b013e3181f61311
4. De Lau LM and Breteler MM. Epidemiology of Parkinson's

disease. Lancet Neurol. 2006;5(6):525-535.
https://doi.org/10.1016/S1474-4422(06)70471-9

5. Bodis-Wollner I, Marx MS, Mitra S, Bobak P, Mylin L and Yahr M. Visual dysfunction in Parkinson's disease. Loss in spatiotemporal contrast sensitivity. Brain. 1987;110(Pt 6):1675-1698.
https://doi.org/10.1093/brain/110.6.1675
6. Matsui H, Udaka F, Tamura A, Oda M, Kubori T, Nishinaka K, et al. Impaired visual acuity as a risk factor for visual hallucinations in Parkinson's disease. J Geriatr Psychiatry Neurol. 2006;19(1):36-40.
https://doi.org/10.1177/0891988705284739
7. Birch J, Kolle RU, Kunkel M, Paulus W and Upadhyay P. Acquired colour deficiency in patients with Parkinson's disease. Vision Res. 1998;38(21):3421-3426.
https://doi.org/10.1016/s0042-6989(97)00398-2
8. Djamgoz MB, Hankins MW, Hirano J and Archer SN. Neurobiology of retinal dopamine in relation to degenerative states of the tissue. Vision Res. 1997;37(24):3509-3529.
https://doi.org/10.1016/S0042-6989(97)00129-6
9. Harnois C and Di Paolo T. Decreased dopamine in the retinas of patients with Parkinson's disease. Invest Ophthalmol Vis Sci. 1990;31(11):2473-2475.
10. Naismith RT, Xu J, Tutlam NT, Snyder A, Benzinger T, Shimony J, et al. Disability in optic neuritis correlates with diffusion tensor-derived directional diffusivities. Neurology. 2009;72(7):589-594.
https://doi.org/10.1212/01.wnl.0000335766.22758.cd
11. Mailankody P, Battu R, Khanna A, Lenka A, Yadav R and Pal PK. Optical coherence tomography as a tool to evaluate retinal changes in Parkinson's disease. Parkinsonism Relat Disord. 2015;21(10):1164-1169.
https://doi.org/10.1016/j.parkreldis.2015.08.002
12. Inzelberg R, Ramirez JA, Nisipeanu P and Ophir A. Retinal nerve fiber layer thinning in Parkinson disease. Vision Res. 2004;44(24):2793-2797.
https://doi.org/10.1016/j.visres.2004.06.009
13. Altintaş O, Işeri P, Ozkan B and Cağlar Y. Correlation between retinal morphological and functional findings and clinical severity in Parkinson's disease. Doc Ophthalmol. 2008;116(2):137-146.
https://doi.org/10.1007/s10633-007-9091-8
14. Moschos MM, Tagaris G, Markopoulos I, Margetis I, Tsapakis S, Kanakis M, et al. Morphologic changes and functional retinal impairment in patients with Parkinson disease without visual loss. Eur J Ophthalmol. 2011;21(1):24-29.
https://doi.org/10.5301/ejo.2010.1318
15. Kirbas S, Turkyilmaz K, Tufekci A and Durmus M. Retinal nerve fiber layer thickness in Parkinson disease. J Neuroophthalmol. 2013;33(1):62-65.
https://doi.org/10.1097/WNO.0b013e3182701745
16. Satue M, Garcia-Martin E, Fuertes I, Otin S, Alarcia R, Herrero R, et al. Use of fourier-domain OCT to detect retinal nerve fiber layer degeneration in Parkinson's disease patients. Eye (Lond). 2013;27(4):507-514.
https://doi.org/10.1038/eye.2013.4
17. Rohani M, Langroodi AS, Ghourchian S, Falavarjani KG, SoUdi R and Shahidi G. Retinal nerve changes in patients with tremor dominant and akinetic rigid Parkinson's disease. Neurol Sci. 2013;34(5):689-693.
https://doi.org/10.1007/s10072-012-1125-7
18. Garcia-Martin E, Rodriguez-Mena D, Satue M, Almarcegui C, Dolz I, Alarcia R, et al. Electrophysiology and optical coherence tomography to evaluate Parkinson disease severity. Invest Ophthalmol Vis Sci. 2014;55(2):696-705.
https://doi.org/10.1167/iovs.13-13062
19. Jiménez B, Ascaso FJ, Cristóbal JA and Del Val JL. Development of a prediction formula of Parkinson disease severity by optical coherence tomography. Mov Disord. 2014;29(1):68-74.
https://doi.org/10.1002/mds.25747
20. Aaker GD, Myung JS, Ehrlich JR, Mohammed M, Henchcliffe C and Kiss S. Detection of retinal changes in Parkinson's disease with spectral-domain optical coherence tomography. Clin Ophthalmol. 2010;4:1427-1432.
https://doi.org/10.2147/OPTH.S15136
21. Archibald NK, Clarke MP, Mosimann UP and Burn DJ. Retinal thickness in Parkinson's disease. Parkinsonism Relat Disord. 2011;17(6):431-436.
https://doi.org/10.1016/j.parkreldis.2011.03.004
22. Albrecht P, Müller AK, Südmeyer M, Ferrea S, Ringelstein M, Cohn E, et al. Optical coherence tomography in parkinsonian syndromes. PLoS One. 2012;7(4):e34891.
https://doi.org/10.1371/journal.pone.0034891
23. Shrier EM, Adam CR, Spund B, Glazman S and Bodis-Wollner I. Interocular asymmetry of foveal thickness in Parkinson disease. J Ophthalmol. 2012;2012:728457.
https://doi.org/10.1155/2012/728457
24. Nguyen-Legros J. Functional neuroarchitecture of the retina: Hypothesis on the dysfunction of retinal dopaminergic circuitry in Parkinson's disease. Surg Radiol Anat. 1988;10(2):137-144.
https://doi.org/10.1007/BF02307822
25. Kumar V, Abbas AK and Fausto N. Cellular adaptations, cell injury and cell death. In: Kumar V and Abbas AK, editors. Robbins and Cotran Pathologic Vasis of Disease. 7th ed. Philadelphia, PA: Saunders; 2006. p. 13.

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