Review Article

Ocular manifestations of Parkinson disease

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ABSTRACT

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder. We aimed to review both the disease and the drug-related ocular manifestations of PD.

Methods: In this manuscript, we have reviewed and summarized existing literature on the ocular manifestations and drug-related complications of PD. We have also discussed the use of current noninvasive imaging techniques, such as optical coherence tomography (OCT), for the early diagnosis and monitoring of PD.

Results: Impaired color vision, reduced stereopsis, reduced contrast sensitivity, pupillary abnormalities, eye movement disorders, convergence insufficiency, dry eye syndrome, glaucoma, visual dysfunctions, retinal abnormalities, and drug-related side effects were among the listed ocular manifestations of PD. There is a large knowledge gap regarding the type of glaucoma affecting PD patients—whether it is open-angle or other types. Further case studies and long-term follow-ups during PD progression are necessary to fill this gap. Patient compliance with follow-up visits for more visual field tests and OCT during PD progression may become problematic when dementia and cognitive impairment occur.

Conclusions: There is a general need for clinicians to perform further tests and more visual examinations to rule out ocular manifestations. Furthermore, additional clinical trials are needed to further evaluate the use of different types of OCT findings as biomarkers of PD progression. This would aid in early diagnosis and in delaying disease progression, if treated promptly.

KEY WORDS

Parkinson's disease, eye movement, ocular manifestations, drug-related ocular complications, biomarkers

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder. PD is thought to be one of the 40 conformational diseases induced by the accumulation of unfolded or misfolded proteins. Improper misfolding and accumulation of unfolded proteins may result in the formation of disordered (amorphous) or ordered (amyloid fibril) aggregates. In PD, amyloidogenic protein accumulation often occurs in the brain tissues with the deposition of alpha-synuclein. Unfolded or misfolded protein aggregation also occurs in different parts of the eye, such as the lens, in case of cataracts [1, 2]. PD is characterized by depletion of dopaminergic neurons in the mid-brain basal ganglia—substantia nigra pars compacta. In addition, owing to the decreased levels of dopamine, motor symptoms also developed, such as resting tremor, bradykinesia, and rigidity. Deposition of α-synuclein and dopamine deficiency in the retina reflects the pathological characteristics of PD in the brain. These findings together support the idea that the eye can act as a gateway to the brain, providing physicians with noninvasive methods for further assessment. Vision is one of the nonmotor systems altered in PD patients. Vision is affected due to decreased dopamine levels, which results in decreased visual

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acuity, impaired contrast and color vision, and decreased retinal nerve fiber layer (RNFL) thickness [3]. Color vision and contrast sensitivity are modulated by the dopaminergic receptors (D1 and D2), which are differentially located in the retinal layers. The absence of dopaminergic receptor activation by dopamine results in signal dispersion and alterations in color vision and contrast sensitivity [4].

Dry eyes, blepharospasm, cataract, diplopia, glaucoma, glaucoma-like visual problems, visuospatial and visuoperceptual impairments, and visual hallucinations are other ocular manifestations of PD [5-8]. Ocular changes, including visual dysfunction, pupil abnormality, lens opacity, and retinal neuronal loss and dysfunction, have been reported in patients with PD. Other manifestations include seborrheic dermatitis and blepharitis [6], lid retraction [9], decreased blinking rate [10], limited upgaze [11], and drug-related adverse effects caused by cholinergic drugs, levodopa, amantadine, and others used in the management of PD. The risk of PD dementia can be evaluated using visual measures and assessment of the retinal structures of the ganglion cell layer and inner plexiform layer in the dopaminergic layers [12]. The study of ocular motor manifestations, particularly eye movements, can help to clarify the evolving clinicopathologic spectrum of disorders of atypical Parkinsonian and can serve as a tool for early detection of PD. The most common oculo-visual problems associated with PD dementia are eye movements, visual hallucinations, visuospatial function, and variations in saccadic eye movement dysfunction, which are valuable diagnostic characteristics for identifying Parkinsonian symptoms [13]. In addition, clinicians should pay special attention to the diagnosis and treatment of glaucoma and dry eye syndrome in patients with PD [14]. Recent research has focused on high-resolution imaging and other technological advancements to increase the sensitivity of ocular motility tests. Eye movements have been studied in clinical care and clinical trials as biomarkers for the diagnosis and progression of PD [15].

The main types of drugs used to treat PD are levodopa (L-DOPA), dopamine agonists, anticholinergics, monoamine oxidase type B (MAO-B) inhibitors, and catechol-O-methyltransferase (COMT) inhibitors. Drug-related complications, such as hallucinations and psychosis, have been reported [16]. Moreover, drug-related ocular manifestations, such as blurred vision, closed-angle glaucoma, and visual hallucinations, have been detected in patients [16]. Finally, convergence insufficiency (CI) has also been reported in cases of idiopathic PD responsive to levodopa [17].

The aim of this manuscript was to review the ocular manifestations of PD and the drugs-related ocular complications, as well as to explore the modalities that are suitable for identifying PD progression.

METHODS

We conducted an electronic search using PubMed and Google Scholar and limited the search to papers in English, with no specific period. We used the following keywords: "Parkinson's Disease", AND "ocular manifestations" of PD including glaucoma, hallucinations, decreased visual acuity, color vision sensitivity, contrast sensitivity, stereopsis impairment, dry eye Syndrome, blepharitis, cataract, diplopia, and pupil abnormalities; "Parkinson's Disease", AND "Eye movement abnormalities" including double vision, color sensitivity, CI, saccade, smooth pursuit eye movement vergence abnormalities, strabismus, reading time (decreased), vertical gaze abnormalities , and rapid eye movement; "Parkinson's Disease" AND "Ocular biomarkers"; as well as, "Parkinson's Disease" AND "drug-related ocular complications", including; hallucinations, psychosis, dopamine-dysregulation syndrome, blurred vision, close-angled glaucoma, and visual hallucinations.

RESULTS

We included original papers that met the following criteria: studies on human subjects, studies that clearly addressed PD (ocular manifestations), and studies that included anti-Parkinsonian agents (drug-related complications). We excluded 2411 articles that were not original research papers, did not have human subjects, evaluated more than one drug treatment (for drug-related complications), or had a trial dose of any anti-parkinsonian agent (for ocular manifestations of PD). Our search retrieved 2509 articles, of which, after considering the stated inclusion criteria and removal of duplicates, 98 articles were finally included in the review. Table 1 summarizes the ocular manifestations of PD. The drug-related complications are summarized in Table 2. The suggestive visual screening tests for each ocular manifestation are summarized in Table 3.

DISCUSSION

PARKINSON'S DISEASE AND OCULAR MANIFESTATIONS

Impaired Color Vision, Low contrast, and Stereopsis

Stereopsis impairment was reported in patients with PD [18] and was closely linked to color perception and motor dysfunction [19]. Impaired color vision and contrast sensitivity was also reported [3, 5, 20, 21].

In addition, the low-contrast charts detected a visual loss in patients with PD, including those with normal visual acuity [22]. In addition, contrast sensitivity is diminished in PD, most at intermediate spatial frequencies [23]. Table 1 summarizes the ocular manifestations of PD.

Table 1. Ocular manifestations of Parkinson's Disease

No	Study and Date	Ocular Manifestations
1	Pfeiffer et al., 2016 [74]	Decreased Visual Acuity
2	Gobel et al., 2014 [3]	Color Vision Sensitivity
3	Weil et al., 2016 [5]	
4	Ekker et al., 2017 [20]	
5	Pieri et al., 2000 [21]	
6	Pfeiffer et al., 2016 [74]	
7	Regan et al., 1984 [22]	Contrast Sensitivity
8	Bulens et al., 1988 [23]	
9	Pfeiffer et al., 2016 [74]	
10	Sun et al., 2014 [19]	Stereopsis Impairment
11	Ekker et al., 2017 [20]	Diplopia
12	Dietz et al., 2011 [24]	Pupil Abnormalities
13	Giza et al., 2011 [25]	
14	Micieli et al., 1991[26]	
15	Biousse et al., 2004 [27]	
16	Fotiou et al., 2009 [28]	
		Oculomotor Abnormalities
17	Pretegiani et al., 2017 [31]	Saccade
18	Jehangir et al., 2018 [35]	Saccade
19	Pretegiani et al., 2017 [31]	Smooth Pursuit Eye Movement
20	Holden et al., 2019 [41]	Convergence Insufficiency
21	Urwyler et al., 2014 [75]	Difficulty with Reading, Diplopia, Floater
22	Kang et al., 2018 [37]	Vergence Abnormalities
23	Kang et al., 2018 [37]	Strabismus
24	Jehangir et al., 2018 [35]	Reading Time (Decreased)
25	Quattrone et al., 2019 [36]	Vertical Gaze abnormalities
26	Biousse et al., 2004 [27]	Blepharospasm
27	Rana et al., 2012 [45]	
28	Yoon et al., 2005 [46]	
29	Reddy et al., 2013 [44]	Dry Eye Syndrome and Lower Blink Rates
30	Borm et al., 2019 [10]	Blepharitis
31	Moreau et al., 2012 [2]	Cataract
32	Lai et al., 2017 [50]	Glaucoma
33	Tsironi et al., 2012 [51]	
34	Bayer et al., 2002 [52]	
35	Yenice et al., 2008 [53]	
36	Crevits et al., 2003 [7]	Visual Dysfunction: Visual Hallucination
37	Ebersbach et al., 1996 [58]	Visual Perception: Directional Bias
38	Crucian et al., 2003 [59]	Visuospatial Dysfunction
39	Regan et al., 1984 [57]	Visual Fatigue was not Reported
40	Satue et al., 2016 [62]	Reduced Thickness and Volume of the Macula
41	Chrysou et al. 2019 [61]	Thinning of the Inner Retinal Layers

Table 2. Drug-related complications in Parkinson's Disease

CLASS	Drug-related complications
Levodopa [17] [78] [79] [83] [85, 86] [87]	 Wearing-off dyskinesia. Cognitive and behavioral problems. Autonomic and psychomotor complications: motor fluctuations, dyskinesia, nausea, and psychosis. Impulse control disorders. Convergence insufficiency. Visual hallucinations, AIEMS (abnormal involuntary eye movements).
Dopamine Agonists [16] [83] [84] [85, 86] [88]	 Cognitive and behavioral problems. Cardiac valve fibrosis. Nausea, vomiting, orthostatic hypotension, confusion, and visual hallucinations. Hallucinations, and psychosis. Impairment of smooth pursuit eye movements and difficulty alternating voluntary gaze shifts.
Monoamine oxidase inhibitors [16] [83]	 Visual hallucinations. Hallucinations and psychosis.
Anticholinergics [83]	Mouth dryness, salivary secretion decreases, blurred vision, constipation, urinary retention, closed-angle glaucoma, sedation, delirium, visual hallucinations, memory loss, nightmares, and confusion.
Amantadine (Anti-viral agent) [83] [89]	 Ankle edema, livedo reticularis, orthostatic hypotension, congestive heart failure, mouth dryness, salivary secretion decreases, blurred vision, constipation, urinary retention, closed-angle glaucoma. Corneal endothelial edema.

Note: The drug-related ocular complications are in colored text.

Table 3. Parkinson's Disease ocular abnormalities and visual tests

Ocular manifestations in PD	References	Visual Tests
Decreased Visual Acuity	[74]	Visual Acuity Test
Color Vision Sensitivity	[3, 5, 20, 21, 74]	Color Vision Test
Contrast Sensitivity	[22, 23, 74]	Contrast Sensitivity Test
Stereopsis Impairment	[19]	Stereopsis Test
Diplopia	[20, 75]	Cover Test
Pupil Abnormalities	[24, 28]	Pupil Test
OCULOMOTOR ABNORMALITIES		
Saccade	[31, 35]	Saccade Test and Reading Time Test
Smooth Pursuit Eye Movement	[31]	Pursuit Test
Convergence Insufficiency	[41, 75]	Binocular Vision Exam
Vergence Abnormalities	[37]	Binocular Test
Strabismus	[37]	Cover Test/ Binocular Vision Exam
Reading Time (Decreased)	[35]	Reading Time Test
Vertical Gaze Abnormalities	[36]	Cover Test and Binocular vision Exam
Blepharospasm	[27, 45, 46]	SLE
Dry Eye Syndrome and Lower Blink Rates	[44]	SLE, Tear Test, Tear Breakup Time Test (TBUT), Blink Rate Test
Blepharitis	[10]	SLE
Cataract	[2]	SLE
Glaucoma	[50-53]	Posterior Segment Exam and OCT of the ON/Anterior Segment OCT for Angle/Fundus Image/IOP measure
Visual Dysfunction: Visual Hallucination	[7, 91-93]	Pareidolia Test Neuropsychiatric Inventory Interview North-East Visual Hallucinations Interview
Visual Perception: Directional Bias	[58]	Visual Perception Test
Visuospatial Dysfunction	[59]	Visuospatial Test
Reduced Thickness and Volume of The Macula	[62]	OCT of Macula
Thinning of the Inner Retinal Layers	[61]	OCT of Retina

Abbreviations: IOP, intraocular pressure; OCT, optical coherence tomography; ON, optic nerve; SLE, slit-lamp examination.

Pupil reactivity

PD patients show normal sympathetic arousal to affective stimuli, which are documented by pupil diameter, but with variations in eye movements [24, 25]. In patients with PD, several signs of abnormal pupil reactivity have been identified. Following light adaptation, the pupil diameters were found to be either larger or unequal in size, and a significant increase in light reflex latency, whereas decreased amplitude, maximum constriction velocity, and maximum acceleration were also observed [25-28].

Moreover, pupillary abnormalities can precede motor symptoms and may occur early in the disease [29]. Pupillary abnormalities are useful as they are potential nonmotor biomarkers for prompt identification and disease progression monitoring in patients with PD due to their modern, quick, non-invasive, and low-cost techniques used for detection [25, 29, 30].

Eye movements

In PD patients, abnormalities are more noticeable in the initial stages of voluntary saccades than reflexive saccades. In advanced stages, the involvement of visually guided saccades is seen. Saccadic hypometria, reduced accuracy, and increased latency are among the most common deficits in PD patients. PD patients often have atypically frequent and large square-wave jerks and impaired reflexive saccade inhibition when voluntary mirror saccades are required. Poor convergence and pursuit are common [31]. Impairment of saccadic and smooth pursuit eye movements has been evident [32], in addition to square-wave jerks and ocular oscillations [33, 34]. Saccadic reading in PD is slower. The reading time was slower in PD with CI by 8 s [35]. In a study, PD patients developed vertical gaze abnormalities, while the diagnosis was changed from PD to progressive supranuclear palsy-Parkinsonism during a 4-year follow-up [36]. In PD patients, vergence abnormalities and strabismus are related to CI, and diplopia has also been reported [37].

Patients with PD and without dementia had prolonged visual fixation duration, which correlated with visual recognition memory tasks. The clinical use of eye movement parameters as an early marker of cognitive decline in PD requires further exploration [38]. The oculomotor cogwheel phenomenon and ocular bradykinesia have been reported as manifestations of extrapyramidal disease [39]. In addition, difficulty in the initiation and execution of movements in PD patients is also mentioned in the literature [40].

Convergence Insufficiency (CI)

Cognitive impairment has been shown to commonly co-occur with CI in Parkinsonian disorders and is associated with significantly greater near point of convergence (NPC) distances [41]. Clinicians should take serious note of cognitive impairment in patients with CI objective findings, whether symptomatic or not. Diplopia has been reported in patients with PD [20, 42]. It is associated primarily with CI [10, 20]. PD patients are reported to have a reduction in vision-related quality of life, which is not associated with visual acuity [43], most likely due to convergence debility.

Dry Eye Syndrome

Signs of dry eyes, abnormal ocular surface staining, and meibomian disease are commonly seen in patients with PD. Patients with PD had lower blink rates and decreased corneal sensitivity. Blink rate correlated with the sensitivity of the corneas, which could be associated with asymptomatic ocular surface disease due to diminished corneal sensitivity. The loss of corneal nerves was not attributed to a lack of corneal sensitivity but was correlated with a diminished blink rate [27, 44]. Blepharitis has also been reported in patients with PD [10]. Blepharospasms has also been reported in patients with PD, which might lead to excessive blinking due to ocular irritation in dry eyes [45, 46].

Glaucoma

Open-angle glaucoma is not a predictor of PD [47-49]. Other studies have found that the occurrence of PD is correlated with a small but statistically significant increase in elderly people with glaucoma [50]. PD patients can show glaucomatous-like perimetric defects, often in the absence of reduced RNFL thickness [51]. In addition, Beyer et al., 2002 concluded that Alzheimer's disease and PD patients may have an increased risk of glaucoma occurrence [52]. Yenice et al. concluded that patients with PD had worse visual field indices indicating a common insult to the nerve fiber, which is the same etiopathogenesis observed in glaucoma and PD [53]. The proposed mechanism underlying this presentation was linked to microorganisms that cause glaucoma via the gut-retina axis, leading to the generation of autoantibodies and autoreactive T cells, which consequently result in autoimmune destruction [54, 55].

Visual Perception, Visual Hallucination, and Visual Fatigue

Several visual dysfunctions in PD are of clinical relevance, such as vague visual complaints, blurred vision, impaired contour perception, distress in a striped surrounding, and visual hallucinations [8, 56]. Errors in visual input processing

could enhance the risk of misinterpretation and even cause visual hallucinations because of various clinical signs, such as misperception of depth, repeated falls, and enhanced motor impairment. It is strongly recommended that all visual deficits be corrected as much as possible. Vision loss should be actively explored and fixed as fast as possible as prolonged visual deficits can be a probable and reversible cause of visual hallucinations [7]. Visual fatigue has not been reported in patients with PD [57].

In addition, the directional bias of initial visual exploration has been reported as a symptom of neglect in PD [58] and visuospatial dysfunction [59].

Retina

In PD, microglia have been reported to play a role in retinal neurodegeneration as a common pathogenic mechanism in PD that plays an important role in neuroinflammation in the form of microglial activation [60]. A meta-analysis of spectral-domain optical coherence tomography (SD-OCT) studies found that PD patients had significant thinning of the inner retinal layers, similar to the changes found in patients with glaucoma and other neurodegenerative diseases [61]. PD can be combined with reduced thickness and volume of the macula [62] and reduced RNFL thickness in the inferior quadrant of the retina [63]. In addition, PD patients retain foveal symmetry between their eyes [64]. The thickness of the retinal layers, visual evoked potentials, and RNFL thickness was similar in both the PD and control groups [65]. There is a correlation between macular thinning, disease progression, and severity in patients with PD [62]. In addition, there is also a link between PD severity and changes in foveal thickness [66]. Few studies using SD-OCT have reported a significant reduction in the inferior peripapillary RNFL thickness, including mean and temporal reduction [67]. There is a major decrease in retinal thickness in the macular area and total macular volume in PD [67-70]. The macular thinning in PD did not show similar differences in the peripapillary RNFL measurements in all studies [71-73].

DRUGS-RELATED COMPLICATIONS

L-DOPA was found to be the most effective treatment for PD since 1960 [76, 77]. The chronic usage of current anti-Parkinsonian medications, in addition to psychomotor and autonomic complications, causes the "wearing-off phenomenon" [78]. Common side effects of motor complications due to levodopa include motor fluctuations and dyskinesia, nausea, psychosis, and impulse control disorders, and related behaviors [79]. Although the therapeutic use of L-DOPA may ultimately be restricted by the development of numerous complications associated with the medication, including response fluctuations, dyskinesia, and psychiatric problems, it is still the drug of choice [80]. Psychosis is typically drug-induced and can be controlled by reducing anti-Parkinsonian prescription therapeutics [77]. Side effects of non-ergot dopamine agonists (Pramipexole) have been reported, including hallucinations, edemas, and drowsiness [81]. Benbir et al. (2006) reported that dopaminergic drugs and levodopa were not related to hallucinations in patients with PD [82].

Anticholinergic medications have both central and peripheral side effects, particularly in elderly patients, which have restricted their significant usage. Some of the adverse effects of these drugs are dry mouth, decreased salivary secretion, blurred vision, constipation, urinary retention, closed-angle glaucoma, sedation, delirium, hallucinations, and memory loss. Finally, anti-Parkinsonian drugs significantly contribute to the onset of these symptoms. This hinders the differentiation between PD progression and the complications associated with drugs [85, 87]. The drug-related complications are summarized in Table 2.

Drug-Related Ocular Complications

As shown in Table 2, ocular complications have been reported following the use of levodopa such as CI and visual hallucinations [17, 85, 86]. Visual hallucinations have been reported using dopamine agonists [83, 85, 86]. Dopaminergic medications were studied during the "ON and "OFF" states in PD; the results showed that during the ON state, mean convergence amplitude and NPC were better than those during the OFF state [43]. In addition, the convergence ability has been reported to be poor in both the "ON" and "OFF" states [43]. Impairment of smooth pursuit eye movements and difficulty in alternating voluntary gaze shifts have been reported in PD patients receiving dopaminergic medications [88].

Visual hallucinations have also been reported using monoamine oxidase inhibitors and anticholinergic agents [83]. Blurred vision and closed-angle glaucoma have been reported with the use of anticholinergics and amantadine (an anti-viral agent) [83].

Levodopa has been shown to cause abnormal involuntary eye movements (AIEMS) in advanced PD patients during the ON state only, while during the OFF state the AIEMS disappeared completely [87]. Amantadine has been reported to cause corneal endothelial edema [89].

VISUAL SCREENING TESTS AND OCULAR BIOMARKERS

Table 3 summarizes the suggestive visual screening tests for each ocular manifestation. Visual acuity, cover, contrast, stereopsis, pupil, and color tests are required for entrance tests to determine visual status and pupil function. Other tests include 3-dimensional (3D) movies on 3D TV tests for stereopsis stimulation rather than the Titmus fly test [90]. Moreover, binocular vision tests, such as positive fusional vergence (PFV) and NPC, are required for CI diagnosis. It has been emphasized that simple reading tasks using 120 single-digit numbers can play the role of a screening tool in clinical practice to assess functional ocular motor difficulties in PD, which can have a considerable effect on the quality of life [35] and electrophysiological recordings such as electrooculogram, flash, pattern and multifocal electroretinogram, or visual evoked potential. An anterior segment slit-lamp examination is needed for dry eyes and cataracts. For glaucoma and retinal evaluation, posterior segment examination is needed and ideally, supported by OCT and fundus imaging. Other tests are also used, such as tear film tests and perimetry [90]. Finally, the Pareidolia test, the Neuropsychiatric Inventory Interview, and the North-East Visual Hallucinations interview are needed to determine visual hallucinations [91-93].

OCT is a non-invasive imaging technique that is used as a potential early biomarkers for the progression of PD [62, 94-96]. The thickness of the RNFL and macular thickness measured by OCT may serve as biomarkers for the early detection and progression of a variety of neurological diseases [62, 94]. In PD, combining retinal structural and functional biomarkers can enhance the diagnostic yield. The tremor could prevent the acquisition of high-quality images. Therefore, non-imaging parameters may also become necessary in cases of advanced disease [95]. OCT-angiography (OCT-A) provides depth-resolution images of blood flow in the optic nerve, choroid, and retina. In the PD cascade, retinal capillary impairment appears to occur early. These findings suggest that OCT-A could represent a new path for PD investigation and will likely be useful in the future as a valuable technique for early disease biomarker detection and for the progression of the disease [96].

Fourier-domain OCT has been shown to be a valid and reproducible device for the detection of subclinical RNFL atrophy in PD patients [62, 65, 97], especially the Spectralis Nsite Axonal Analytics Module. Given the large similarity between the measurements of the two instruments, there was a significant difference between the Cirrus and Spectralis devices in the RNFL thickness measurements [97]. As a possible biomarker for PD diagnosis, RNFL thickness and the inner layers of the macular area have been used [66].

Without any visible changes in the routine ophthalmological examination, visual deficits may occur in PD, which can explain why electrophysiological recordings are needed at least partially to evaluate visual dysfunction during PD [14]. In addition, the development of early biological markers of saccadic eye movements for specific pathophysiological states, such as saccadic eye movement circuitry includes both cortical and subcortical brain regions, and saccadic task manipulation offers insight into information processing in the impaired brain. A brain functioning at different levels in PD can be determined by reflexive and voluntary saccadic tasks [98].

This study had some limitations. First, it was analyzed by one author, which may have led to bias. The strength of this study was that it included all the ocular manifestations and the required visual tests during the exam, which makes it easier for clinicians to use in the examination room. In addition, it highlighted the need for more future studies on PD ocular manifestations, as for certain ocular manifestations, there was only one reference. Further studies are required to determine whether accommodation is impaired in PD. Additional case studies are also required in this area.

CONCLUSIONS

There is a huge knowledge gap regarding the type of glaucoma that occurs in PD—whether it is open-angle glaucoma or other types. This gap needs to be filled via further case studies and longitudinal reports of PD progression. Problems with patient compliance with the follow-up visits to perform more visual field tests and OCT, as PD progresses, dementia, may arise as cognitive impairment develops. Finally, we concluded that there is a general need for clinicians to conduct further tests, and for the awareness of the necessity to include the listed visual examinations and visual tests to rule out ocular manifestations in PD. In addition, more clinical trials are needed to further evaluate the different types of OCT as biomarkers in PD progression, as this would aid in early diagnosis and delay the potential progression of the disease if treated early.

ETHICAL DECLARATIONS

Ethical approval: This study was a review and no ethical approval was required.
Conflict of interest: None.

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