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Review Article

Ocular Findings in Patients with Parkinsonism: A Narrative

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Received: December 11, 2023; **Published:** January 18, 2024

Abstract

Eyes are windows to the brain. Patients with neurodegenerative movement disorders have some characteristic eye signs which are either exclusive to these disorders or shared amongst various disorders. This narrative highlights various eye signs seen in patients with parkinsonism.

Keywords: *Parkinsonism; Parkinson's Disease (PD); Alpha-Synucleinopathy; Visual Acuity; Blepharospasm; Altered Tear Film; Xerophthalmia*

Introduction

Parkinson's disease affects 1 - 2% of the population over 60 years of age [1]. Parkinson's disease (PD) is an alpha-synucleinopathy that leads to prominent motor symptoms including tremor, bradykinesia and postural instability. Patients with PD also have non-motor symptoms. Similarly, motor and non-motor involvement of the eyes occur in parkinsonian spectrum disorders ranging from visual symptoms in the form of decreased visual acuity, blepharospasm, altered tear film and xerophthalmia, color vision abnormalities, visual hallucinations, ocular motility disorders, reduced bink rate, retinal degeneration etc [2]. The purpose of this narrative is to highlight the ocular involvement in patients with parkinsonism.

Literature search

The literature was thoroughly searched from "PubMed" and "Google Scholar" database using keywords "Eye signs in parkinsonism" OR "Ocular manifestations in parkinsonism" from year 2018 to 2023. Search results yielded 258 results. After excluding texts in language other than English, only abstracts and not matching the context, 14 studies were included in the literature review.

The ocular manifestations in patients with Parkinson's disease are discussed below:

- **Ocular surface abnormalities (Including eye lid, cornea and conjunctiva):** Changes on the ocular surface, mostly related to dry eyes and decreased blink frequency, are another typical observation in Parkinson's disease patients. PD patients' tears exhibit distinct modifications associated with protein composition, and *in vivo* confocal imaging has revealed significant abnormalities in many corneal layers in this context. These alterations can be linked to the illness itself as well as the drugs used to treat it. PD patients using amantadine, in particular, have well-documented symptoms of corneal toxicity, both at the epithelial and endothelial

levels, in the literature. The literature contains case reports of corneal edema and the ensuing corneal opacity. When compared to controls, PD patients show noticeably lower BR, corneal thickness, Tear breakup time (TBUT), and tear production. These results underscore the potential for dry eye illness and Parkinson's disease to coexist, underscoring the importance of screening and suitable therapies for doctors who treat PD patients. Several PD biomarkers, including α-synTotal and α-synOligo, catecholamines, α-2-macroglobulin, and other proteins implicated in oxidative stress, lipid metabolism, and immunological response, are present in tears as demonstrated in recent research [2].

- **Pupil:** Anisocoria, increased pupil constriction time and prolonged constriction, delayed reflex constriction or larger pupil diameters can be seen in patients with PD. On the contrary, small constriction amplitudes may be found [3].
- **Retina:** Color discrimination, contrast sensitivity, and visual acuity are among the many visual symptoms that are attributed to impaired high-level visual processing; however, patients with Parkinson's disease also exhibit abnormalities in retinal structure and function. In fact, according to a cohesive theory of the visual pathway, abnormalities originating in the retina may provide aberrant input to the visual cortex, thereby impacting various functions including visual acuity, contrast sensitivity, color vision, motion perception, and visuospatial construction. Existing reports using OCT describe retinal nuclear layer thinning, fundus-retinal thickness, fundus volume, and intermediate retinal nerve fiber layer (RNFL) in patients with Parkinson's disease compared to healthy matched participants. Decreased RNFL thickness and changes in visual fields, visual evoked response (VER) and pattern ERG (pERG) in patients [4].
- **Vision:** The disease also determines changes in the visual pathway, because dopamine is present in the amacrine cells of the internal plexiform layer of the retina and has several functions in the eye. In fact, it is involved in light adaptation, spatial contrast sensitivity, color discrimination, eye motor control, and the photoreceptor regeneration process, and is also probably involved in the cyclic regulation of intraocular pressure and has an apoptotic role [5].
- **Eye movements:** Optical motility examination should include bedside evaluation and laboratory recording of optical misalignment, range of eye movements, involuntary eye movements, nystagmus, saccades, smooth pursuit (SP), the vestibulo-optical reflex (VOR), optokinetic nystagmus (OKN), and vergence eye movements. A moderate restriction of upward aspect is common in senior individualities with or without parkinsonism. Involuntary eye movements include nystagmus or broken saccades. In general, ocular motor deficits in PD are not as prominent as in progressive supranuclear palsy syndrome (PSPS) or Huntington's disease (HD) and often require laboratory tests to detect abnormalities. In PD, sustained fixation can be interrupted by saccadic intrusions, such as SWJs, which are characterized by involuntary saccadic movements from the fixation point and back to the fixation point with a distance of approximately 200 ms and an amplitude of 0.5 - 5°. SWJs can be observed in normal elderly subjects, but frequent and large SWJs in PD have been associated with compensatory increased activity in the anterior eye field.

Saccades are usually hypometric, especially vertically. Downward gaze paresis is not seen in PD, and when present, a diagnosis of progressive supranuclear palsy-Richardson syndrome (PSP-RS) should be considered. Most patients with PD have difficulty making self-paced saccades between two continuously visible objects. When patients are verbally instructed to look between two different objects, PD patients typically make near-accurate saccades. However, when asked to maintain this activity independently, their saccades invariably become hypometric. Hypometric voluntary saccades are hypothesized to result from increased inhibition of the superior colliculus (SC) and eye precession due to dysfunction of the frontal-basal ganglia-SC circuits. However, reflexive saccades can be generated by direct projections from the parietal cortex to saccade-related neurons in the SC interlayer. Latency and speed of reflexive saccades are usually normal in PD. Because inhibition of reflexive saccades to visual stimuli is impaired in PD patients, antisaccade testing can reveal abnormal executive function even in the early stages of PD. In one study, anti-saccade errors were associated with freezing of gait, and increased latency was associated with impaired postural control. Impaired inhibition of unwanted saccades may be related to dopaminergic reduction in the prefrontal cortex, leading to a lack of SC suppression of the basal ganglia. SP is usually impaired in PD. Combined head tracking is abnormal in the same way as SP, when the head is present in most PD patients. Although low-frequency rotational and caloric

responses may be impaired in PD patients, VOR gain is close to 1.0 at higher head rotational frequencies, consistent with natural activity, particularly visual fixation. Patients also exhibit abnormal eyelid movements, including decreased blinking, eyelid retraction, and drooping eyelids. Unlike patients with PSP-RS, patients with PD follow their blink response when the flashlight is flashed repeatedly. Treatment with levodopa can improve saccadic accuracy, SP, and convergence insufficiency. Electrical stimulation of the pallidum or subthalamic nuclei has been reported to improve performance in memory-guided or antisaccade tasks [6].

S. No.	Type of study	Year	Sample size	Results	Reference
1.	Longitudinal Follow-up Study	2022	12	Progressive loss of thickness of the outer retinal layer on serial evaluation	[7]
2.	Cross-sectional study	2019	20	Slowing, interruptions, and curvatures in the saccade trajectory	[8]
3.	Cross-sectional study	2020	8	In PD, dopaminergic amacrine cell number was reduced between 58% and 26% in different retinal regions, involving a decline in the number of synaptic contacts with AII amacrine cells (by 60%) and melanopsin cells (by 35%)	[9]
4.	Experimental/Interventional Study	2018	20	In the visual memory task, DBS increased the amplitude of saccades scanning simple but not complex drawings. In the visual search tasks, DBS showed no effect on saccade amplitude or frequency	[10]
5.	Case control study	2021	33	PD group had increased pupillary response with increased postural demand compared to the healthy controls	[11]
6.	Case control study	2021	14	The latency of disparity-driven vergence onset was significantly longer for patients with PD compared with healthy controls	[12]
7.	Pilot case control study	2019	36	Tear protein level alterations	[13]
8.	Case control	2019	30	Involvement of retinal layers, in particular the peripapillary retinal nerve fiber layer (RNFL) and macular ganglion cell complex (mGCC)	[14]
9.	Case Report	2021	1	Early-onset PD patient carrying a GBA mutation presenting levodopa induced ocular dyskinesia	[15]
10.	Review article	2018	-NA-	In Parkinson's disease, the evidence suggests that strabismus is related to convergence insufficiency; however, it is responsive to dopamine replacement therapy and can, therefore, fluctuate with medication "on" and "off" periods throughout the day	[16]

11.	Review article	2020	-NA-	co-expression of PD and RBD is characterized by non-tremor predominant subtype and higher incidence of freezing	[17]
12.	Cross sectional study	2022	43	Decreased vision associated with reading difficulty (40%) was common in PD patients. In terms of gaze restriction, vertical gaze involvement (35%) was more than horizontal involvement (7%). Convergence insufficiency (CI) was the most common binocular vision dysfunction (30%), followed by CI with oculomotor dysfunction (14%) and vertical gaze palsy (18%)	[18]
13.	Review article	2023	NA	Dry eyes, blepharospasm, reduced blink rate, saccadic eye movement abnormalities, smooth pursuit deficits, and impaired voluntary and reflexive eye movements. Furthermore, visuoperceptive impairments affect the ability to perceive and recognize visual stimuli accurately	[19]
14.	Systematic Review	2021	NA	PD patients have SPEM abnormalities	[20]

Table 1: *Summarizes the findings of studies on ocular manifestations in patients with Parkinson's disease done within 2018-2023.*

Conclusion

Greater awareness and early recognition of ocular and visual problems in PD might enable timely instalment of tailored treatments, leading to improved patient safety, greater independence, and better quality of life.

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Volume 15 Issue 2 February 2024