Ocular and Visual Complications of Parkinson's Disease

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Optometry's Meeting 2023
Washington DC

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Financial Disclosures - Dr. Theis

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All risks have been mitigated

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Objectives

- Review the epidemiology and pathophysiology of Parkinsons Disease
- Outline the different ocular health, oculomotor, and visual processing disorders that can occur in Parkinsons disease
- Discuss ocular side effects of Parkinsons medications and deep brain stimulation and offer methodologies for how to discuss co-management of these cases with neurology when they occur
- How to differentiate the difference between Parkinsons disease and Progressive Supranuclear Palsy and Multiple System Atrophy using the oculomotor system

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Parkinson's Disease - Epidemiology

- 2nd Most common neurodegenerative disorder after Alzheimer's disease
- More prevalent in Western countries (Europe, North America, South America) than Eastern Countries (African, Asian, Arabic)
  - 1 million in US, 10 million worldwide
  - Prevalence all ages
    - Western countries 66-1500 per 100,000
    - Eastern 10-43 per 100,000
- Incidence 10-18 per 100,000 person-years
- More prevalent in Hispanic/Latinos, Caucasians than Asians and African ethnicities
- Male: Female 3:2
- More common with increasing age (1% at age 60 and 4% by age 80)

Abbas MM, Xu A, Tan LCS. Epidemiology of Parkinson's Disease – East Versus West. *Mov Disord Clin Pract*. 2018;5(1):14-28
Kalia LV, Lang AE. Parkinson's Disease. *Lancet*. 2015;386(9996):896-912

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Parkinson's Disease - Pathophysiology

- Neurodegenerative disease
- Early death of dopaminergic neurons in substantia nigra (extrapyramidal region of the brain)→ dopamine deficiency in basal ganglia→uncontrolled excitatory impulses and movement disorder
- Lewy pathology – aggregation of abnormally folded proteins in cell body and processes of neurons

Kalia LV, Lang AE. Parkinson's Disease. *Lancet*. 2015;386(9996):896-912

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Parkinson's Disease - Etiology

Etiology – unknown

- Combination of genetic and environmental factors – but rarely hereditary

Environmental Risk Factors

- Increased Risk
  - Pesticide/herbicide exposure
  - History of traumatic brain injury
  - Rural living
  - Beta blocker use
  - *Exposure to metals, solvents-polychlorinated biphenyls (Trichloroethylene), antipsychotics*
- Decreased risk
  - Smoking
  - Caffeine intake
  - NSAID
  - Calcium channel blocker
  - Physical Activity
  - *Alcohol consumption*

Abbas MM, Xu A, Tan LCS. Epidemiology of Parkinson's Disease – East Versus West. *Mov Disord Clin Pract*. 2018;5(1):14-28
Kalia LV, Lang AE. Parkinson's Disease. *Lancet*. 2015;386(9996):896-912

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Genetics

- 15% of people with PD have family history

- SNCA – makes alpha-synuclein (gathers in clumps – lewy bodies), AD
- PARK2 – makes parkin (normally helps cells break down and recycle proteins), AR
- PARK7 – makes protein DJ-1 (protects against mitochondrial stress), AR
- PINK1 - makes protein kinase that protects mitochondria from stress, AR
- LRRK2 – Makes protein kinase, AD

AR= Autosomal Recessive AD = Autosomal Dominant

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Systemic Manifestations of Parkinson's Disease

NO two people experience Parkinson's disease the same way

Motor
- Resting tremors
- Muscular rigidity
- Bradykinesia
- Impaired balance
- Difficulty swallowing, drooling
- Postural and gait impairment
  - Shuffling gait
  - Freezing of gait and falls
- Inability to rotate the neck and trunk
- Dysphagia and speech dysfunction

Non-motor (usually present before motor symptoms)
- Olfactory dysfunction
- Cognitive impairment
- Psychiatric symptoms (mood disorder, depression)
- Sleep disorders
- Autonomic dysfunction (urinary incontinence, constipation)
- Dementia
- Pain
- Fatigue
- Visual symptoms

Kalia LV, Lang AE. Parkinson's Disease. *Lancet*. 2015;386(9996):896-912

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Why Vision sequelae is important in Parkinson's

- Visuopatial impairment → important predictor of dementia in PD (Weil)
- Visual hallucinations → important predictor for admission to assistive living
- Ocular and visual disorders reduces quality of life
  - Vexing problem because PD patients have problems with internally guided movements and postural control, which they compensate for with visual movements
- Visually impaired have increased fall rates
  - 80% of PD patients who fell within 1 year timeframe were visually impaired vs 66% of non-fallers (Wood)
  - Identification can help prevent falls/injuries, increase independence and QOL
- Can use vision to improve motor symptoms
  - Visual cueing (stationary stripes pasted onto the floor) is an evidence-based neurorehab technique to alleviate freezing of gait (Nieuwboer and Nonnekes)
- Visual sequelae diagnosis can help differentiate between Parkinson's disease and Progressive supranuclear palsy (PSP) and multiple system atrophy (MSA) (Biosse)
- Visual sequelae may present in the prodromal state and be a useful biomarker for PD diagnosis and progression

V. Biousse, B.C. Skibell, R.L. Watts, D.N. Loupe, C. Drews-Botsch, N.J. Newman, Ophthalmologic features of Parkinson's disease, Neurology 62 (2004) 177e180.
R.S. Weil, A.E. Schrag, J.D. Warren, S.J. Crutch, A.J. Lees, H.R. Morris, Visual dysfunction in Parkinson's disease, Brain 139 (2016) 2827e2843.
B.H. Wood, J.A. Bilclough, A. Bowron, R.W. Walker, Incidence and prediction of falls in Parkinson's disease: a prospective multidiscipllnary study, J. Neurol. Neurosurg. Psychiatry 72 (2002) 721e725.
A. Nieuwboer, G. Kwakkel, L. Rochester, D. Jones, E. van Wegen, A.M. Willems, F. Chavret, V. Hetherington, K. Baker, I. Lim, Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial, J. Neurol. Neurosurg. Psychiatry 78 (2007) 134e140.
J. Nonnekes, A.H. Snijders, J.G. Nutt, G. Deuschl, N. Giladi, B.R. Bloem, Freezing of gait: a practical approach to management, Lancet Neurol. 14 (2015) 768e778.

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Parkinsonian Disorders

- Parkinson disease
- Atypical Parkinsonian syndromes
  - Progressive supranuclear palsy (PSP)
  - Multiple System Atrophy (MSA)
  - Corticobasal syndrome (CBS)
  - Dementia with Lewy bodies (DLB)
- Distinct ocular and oculomotor disorders may aid in facilitating diagnosis
- Becoming increasingly important as newer medications on the horizon necessitate appropriate diagnosis and triage

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Ocular and Visual Abnormalities in PD

Afferent Visual Pathway (Eyelid/Eyeball)	Efferent Visual Pathway (Oculomotor)	Higher Order Visual Pathway (Cortical)
• Eyelids • Tear Ducts • Cornea • Lens • Pupil • Retina • Macula • Optic Nerve	• Convergence • Smooth pursuits • Saccades • Vertical gaze impairment (up>down) • Fixation (nystagmus) • Ocular tremor • Dyskinetic eye movements	• Visual hallucinations • Visuospatial deficits • Impaired facial expression recognition

Ekker MS et al. Ocular and visual disorders in Parkinsons disease: Common but frequently overlooked. Parkinsonism and related disorders. 2017:40:1-10.

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Eyelids in PD and Variants

- Eyelid apraxia (PSP>MSA>PD)
- Decreased spontaneous blink rates
- Blepharospasm
- Eyelid Retraction (PSP>PD)
- Superior eyelid ptosis (PARK2)
- Meibomian gland disease

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Pathophysiology of Blinking

- Primary muscle of eyelid closure is the orbicularis oculi (CN7)
- Mechanism
  - Levator stops firing while palpebral (but not orbital) portion of orbicularis oculi contracts → active eyelid closure
  - Once closure is complete, OO stops firing and basal level of levator resumes (eyelid opens)
- Pathoanatomy
  - Superior colliculus → facial motor nucleus and supraoculomotor area over the central caudal nucleus (CCN)
    - SC also gets afferent input from trigeminal sensory nucleus (tactile eyelid/corneal reflex) and dorsal midbrain (light reflex)
    - SC is inhibited by the pars reticulata of substantia nigra through dopaminergic projections in the nigra-collicular pathway

Esteban A, Salinero E. Reciprocal reflex activity in ocular muscles: implications in spontaneous blinking and Bell's phenomenon. Eur Neurol (1979) 18:157–65. doi:10.1159/000115072
Schmidtke N, Buttner-Ennever JA. Nervous control of eyelid function: a review of clinical, experimental, and pathological data. Brain (1992) 115:227–47. doi:10.1093/brain/115.1.227
Gnadt JW, Lu SM, Breznen B, Basso MA, Henriquez VM, Evinger C. Influence of the superior colliculus on the primate blink reflex. Exp Brain Res (1997) 116:389–98. doi:10.1007/PL00005767
Basso MA, Powers AS, Evinger C. An explanation for reflex blink hyperexcitability in Parkinson's disease. I. Superior colliculus. J Neurosci (1996) 16(22):7308–17

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Spontaneous Blinking

- Mean blink rate 19.74 +/-9.12 per min… 15-20, higher in women than men
- Mean blink rate with reading a book 11.35 +/-10.20 per min
- Mean blink rate with reading a tablet 14.93 +/-10.90 per min
- PD - reduces by 30% ~ 4.5-6 blinks/min
- PSP – significantly reduces to 3 blinks/min

- Spontaneous eye blink rate (EBR) is correlated to dopamine levels in the brain, may be useful for predicting motor status in patients with PD
  - non-invasive indirect marker of central dopamine function
  - Levodopa and DBS increase EBR

Abusharha, Ali A. "Changes in blink rate and ocular symptoms during different reading tasks." *Clinical optometry* vol. 9 133-138. 20 Nov. 2017, doi:10.2147/OPTO.S142718
Bologna M, Fasano A, Modugno N, Fabbrini G, Berardelli A. Effects of subthalamic nucleus deep brain stimulation and L-DOPA on blinking in Parkinson's disease. Exp Neurol. 2012 May;235(1):265-72. doi: 10.1016/j.expneurol.2012.02.004. Epub 2012 Feb 14. PMID: 22366535.
Korosec M, Zidar I, Reits D, Evinger C, Vanderwerf F. Eyelid movements during blinking in patients with Parkinson's disease. Mov Disord (2006) 21(8):1248–51. doi:10.1002/mds.20930
Sforza C, Rango M, Galante D, Bresolin N, Ferrario VF. Spontaneous blinking in healthy persons: an optoelectric study of eyelid motion. Ophthalmic Physiol Opt (2008) 28(4):345–53. doi:10.1111/j.1475-1313.2008.00577.x
Biousse V, Skibell BC, Watts RL, Loupe DN, Drews-Botsch C, Newman NJ. Ophthalmologic features of Parkinson's disease. Neurology (2004) 62(2):177–80. doi:10.1212/01.WNL.0000103444.45882.D8
Golbe LI, Davis PH, Lepore FE. Eyelid movement abnormalities in progressive supranuclear palsy. Mov Disord (1989) 4(4):297–302. doi:10.1002/ mds.870040402

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Reflexive Blinking

- Inverse relationship between dopamine and reflex blinking so reduced dopamine would lead to increased reflexive blinking
- Myerson's sign – trigeminally mediated blink in response to taping the forehead
  - Normally habituated
  - Can occur in PD and other structural, metabolic and degenerative disorders
- Increased blinking to light (PSP>PD)
- Blepharospasm – overactivity of reflexive blinking

Brodsky H, Dat Vuong K, Thomas M, Jankovic J. Glabellar and palmomental reflexes in parkinsonian disorders. Neurology (2004) 63(6):1096–8. doi:10.1212/01.WNL.0000140249.97312.76 57. Kuniyoshi S, Riley DE, Zee DS, Reich SG, Whitney C, Leigh RJ. Distinguishing progressive supranuclear palsy from other forms of Parkinson's disease: evaluation of new signs. Ann N Y Acad Sci (2002) 956:484–6. doi:10.111 1/j.1749-6632.2002.tb02862.x

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Blepharospasm

- Focal dystonia
- Involuntary, bilateral, synchronous, symmetrical contraction of orbicularis oculi muscles (preseptal and pretarsal)
- Decreased spasms and blink rate (increased eyes open) with reading and writing vs speaking
  - Occipital cortical activation may modulate orbicularis oculi spasms and blink response through the basal ganglia to reduce activity in the trigeminal blink reflex circuit
- DDx
  - Tics
  - Hemifacial spasm (unilateral, microvascular compression of facial nerve)
  - Meige syndrome (involuntary contraction of both upper and lower face)
  - Apraxia of eyelid opening (inability to open eyes)
- Tx
  - Botox
  - Orals: Benzodiazepines, anticholinergics, tetrabenazine, baclofen

Defazio G, Hallett M, Jinnah HA, et al. Blepharospasm 40 years later. Mov Disord 2017; 32:498–509
Ferrazzano G, Conte A, Belvisi D, et al. Writing, reading, and speaking in blepharospasm. J Neurol 2019; 266:1136–1140.

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Dry Eye Disease in PD

- Prevalence 53-60% in patients with Parkinson's Disease
  - Vs. 5-35% of general population (50yo+)
- Pathophysiology
  - Decreased blink rate → reduced lipid distribution→ increased aqueous evaporation
  - Decreased tear production due to autonomic (parasympathetic) innervation to lacrimal gland
- You need to ask!
- You need to test!
  - Corneal desensitivity
  - Schirmer's
  - TBUT
  - Blink Rate
    - Normally blink rate decreases with saccades, in PD and PSP it increases
- You need to treat!

E.S.o.t.I.D.E. WorkShop, The epidemiology of dry eye disease: report of the epidemiology subcommittee of the international dry eye WorkShop (2007), Ocul. Surf. 5 (2007) 93e107.
C. Tamer, I.M. Melek, T. Duman, H. Oksuz, Tear film tests in Parkinson's disease patients, Ophthalmology 112 (2005) 1795.

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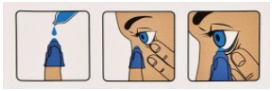
Dry Eye Disease in PD

- Artificial tears – watch them put them in
  - Try eye drop devices
  - Think sprays!
  - Punctal Plugs



E.S.o.t.I.D.E. WorkShop, The epidemiology of dry eye disease: report of the epidemiology subcommittee of the international dry eye WorkShop (2007), Ocul. Surf. 5 (2007) 93e107.
C. Tamer, I.M. Melek, T. Duman, H. Oksuz, Tear film tests in Parkinson's disease patients, Ophthalmology 112 (2005) 1795.

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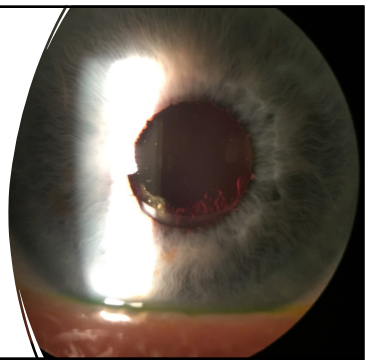
PD and the Lens

- Cataracts – increased rates of nuclear sclerosis and posterior subcapsular cataracts, particularly in patients with dementia



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PD and the Pupil

- Larger pupil diameter after light adaptation
- Reduced amplitude of contraction
- Prolonged contraction time at light reflex
- Mainly involving the parasympathetic system
- Spontaneous changes in pupil diameter is positively associated arousal symptoms (sleepiness)
  - May be a nonmotor marker of progression in PD

Micieli G, Tassorelli C, Martignoni E, Pacchetti C, Bruggi P, Magri M, Nappi G. Disordered pupil reactivity in Parkinson's disease. Clin Auton Res. 1991 Mar;1(1):55-8. doi: 10.1007/BF01826058. PMID: 1821667.
Jain S, Siegle GJ, Gu C, Moore CG, Ivanco LS, Studenski S, Greenamyre JT, Steinhauer SR. Pupillary unrest correlates with arousal symptoms and motor signs in Parkinson disease. Mov Disord. 2011 Jun;26(7):1344-7. doi: 10.1002/mds.23628. Epub 2011 Apr 19. PMID: 21506163; PMCID: PMC3119728.

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Reduced Dopaminergic Activity and the Eye

- Retinal dopamine is synthesized in and released by amacrine cells
- Dopamine release is triggered by light input and is related to retinal circadian rhythm (light adaptation), cell survival and eye growth
- Visual Symptoms in PD
  - Visual dimness
  - Blur
  - Double Vision
  - Hallucinations
- Visual Signs in PD
  - Reduced visual acuity
  - Reduced contrast sensitivity
  - Reduced color discrimination

Archibald NK, Clarke MP, Mosimann UP, Burn DJ. The retina in Parkinson's disease. *Brain*. 2009;132:1128-1145
Ekker MS, Janssen S, Seppi K et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. *Parkinsonism and Related Disorders*. 2017;40:1-10.

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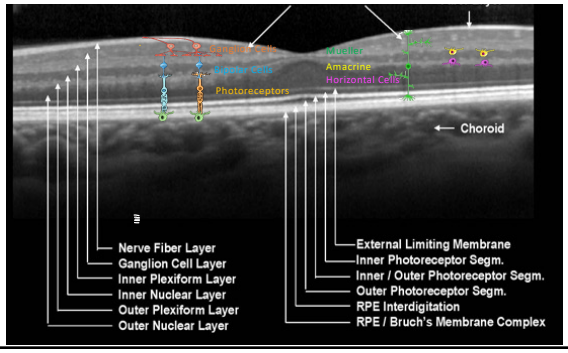

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Cell Types in the Retina - Supportive

- Supportive Cells
  - Amacrine Cells – intermediate cells, 42 types
    - Release inhibitory neurotransmitter – GABA or glycine, some release dopamine
    - Synapses with bipolar cells, dendrites, and soma of ganglion cells
    - Modulates information that reaches the ganglion cells
  - Horizontal Cells – 3 types
    - GABAergic interneurons – inhibitory input to bipolar/photoreceptor cells
    - Synapse with photoreceptors bipolar cells and other horizontal cells
    - Modulate the cone response
  - Interplexiform neurons
    - Found in later of amacrine cells

Mahabadi N, Al Khalili Y. Neuroanatomy, Retina. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK545310/

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Reduced Dopaminergic Activity and the Eye

- Reduction in retinal dopamine results in reduced contrast sensitivity
- Retina (LGN/Visual Cortex)
  - RNFL thinning
    - Gradually diminishes as PD progresses
    - Can be asymmetric (PD can be asymmetric)
  - Reduced macular volume, thinner/broader foveal pit

Archibald NK, Clarke MP, Mosimann UP, Burn DJ. The retina in Parkinson's disease. *Brain*. 2009;132:1128-1145
Ekker MS, Janssen S, Seppi K et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. *Parkinsonism and Related Disorders*. 2017;40:1-10.

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Glaucoma and Parkinson's disease

- Increased prevalence of primary open-angle glaucoma 16-24% in PD compared to 7% of controls
- Pathophysiology for open-angle?
  - Progressive retinal dopamine depletion → retinal nerve fiber layer loss and
  - Alpha-synuclein mediated axonal degeneration
- Angle-closure glaucoma – more due to pre-existing narrow angles and dopaminergic/anticholinergic medication

B. Nowacka, W. Lubinski, K. Honczarenko, A. Potemkowski, K. Safranow, Ophthalmological features of Parkinson disease, Med. Sci. Monit. 20 (2014) 2243e2249.
A.U. Bayer, O.N. Keller, F. Ferrari, K.P. Maag, Association of glaucoma with neurodegenerative diseases with apoptotic cell death: Alzheimer's disease and Parkinson's disease, Am. J. Ophthalmol. 133 (2002) 135e137.

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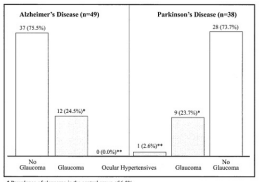
Glaucoma and Neurodegenerative disease?

"Patients with Alzheimer's disease and Parkinson's disease may have an increased occurrence rate of glaucoma."



- Glaucomatous visual field defects or cup-to-disk ratios of 0.8 or greater were recorded in 12 patients with Alzheimer's disease (24.5%) and in 9 patients with Parkinson's disease (23.7%).

Bayer AU, Keller ON, Ferrari F, Maag KP. Association of glaucoma with neurodegenerative diseases with apoptotic cell death: Alzheimer's disease and Parkinson's disease. *Am J Ophthalmol.* 2002; 133: 135–137.

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Is it really Glaucoma?

- METHODS: Retrospective chart review (observational case series). The ophthalmologic charts of 49 patients with Alzheimer's disease and of 38 patients with Parkinson's disease were reviewed to determine the occurrence rate of glaucoma among these patients.
- The diagnosis of probable glaucoma required at least one of the following two criteria:
  - A characteristic pattern of glaucomatous visual field loss;
  - A cup-to-disk ratios of 0.8 or greater with an optic nerve head appearance consistent with glaucoma.
  - All patients with Alzheimer's disease were examined by two of the investigators (A.U.B., O.K.N.) with subspecialty training in glaucoma. In no instance was the diagnosis of glaucoma dependent on the level of intraocular pressure. A
- Ocular hypertension with intraocular pressure readings exceeding 23 mm Hg was not recorded in patients with Alzheimer's disease (0%) but in one patient with Parkinson's disease (2.6%).

Bayer AU, Keller ON, Ferrari F, Maag KP. Association of glaucoma with neurodegenerative diseases with apoptotic cell death: Alzheimer's disease and Parkinson's disease. *Am J Ophthalmol.* 2002; 133: 135–137.

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OPEN ACCESS

Eye Movements, Strabismus, Amblyopia and Neuro-ophthalmology | August 2016

In Vivo Morphology of the Optic Nerve and Retina in Patients With Parkinson's Disease

Anastasia Pilat; Rebecca J. McLean; Frank A. Proudlock; Gail D. E. Maconachie; Viral Sheth; Yusuf A. Rajabally; Irene Gottlob

August 2016
Volume 57, Issue 10
‹ ISSUE ›

+ Author Affiliations & Notes

Investigative Ophthalmology & Visual Science August 2016, Vol.57, 4420-4427. doi:https://doi-org.libproxy.berkeley.edu/10.1167/iovs.16-20020

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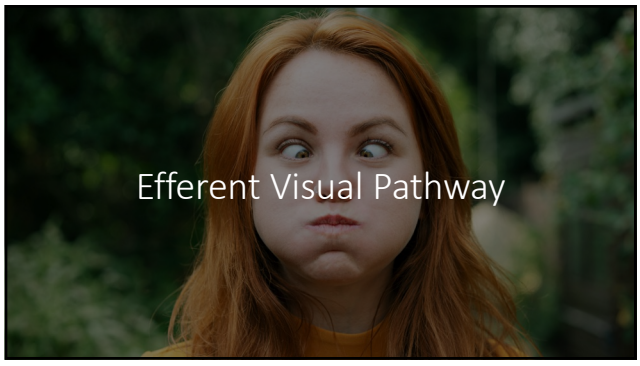

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Why do we care about eye movements?

1. Bring a visual target of interest onto the fovea
   1. Saccades - fast moving target
   2. Smooth pursuits – slow moving target
   3. Vergences – near/far moving target
2. Maintain a visual target on the fovea under various conditions (target/head/body movement)
   1. Fixation – continually maintain eye position
   2. Compensatory eye movements during head/body movements
      1. Vestibular-ocular reflex (VOR)
      2. Optokinetic

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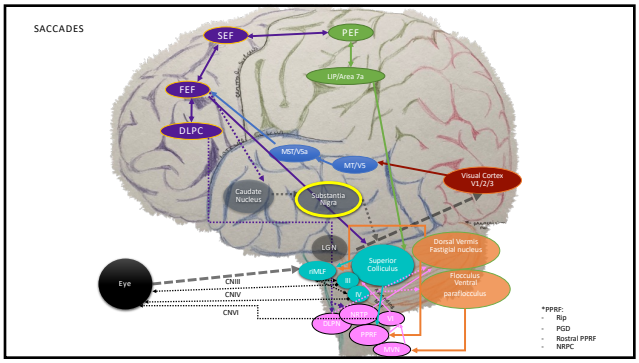

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Eye Movements and Anatomy

	Fixation	VOR	OKN	Saccades	Smooth Pursuits	Vergences*
Brainstem	X	X	X	X	X	X
Cerebral Cortex	X			X	X	X
Cerebellum		X		X	X	X
Basal Ganglia	X				X	?
Superior Colliculus	X					
Vestibular sensors (Semicircular Canals, Otoliths)		X				

Pelak V. Ocular Motility of Aging and Dementia. Curr Neurol Neurosci Rep (2020): 10:440-447)

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Oculomotor Manifestations of Parkinson's Disease

- Prolonged fixation
- Saccadic dysmetria
  - Prolongs reading speed
  - Antisaccades abnormal – can be used as cognitive predictors of decision-making, visual memory, and visual search ability
  - Associated with freezing of gait
- Abnormal Smooth pursuit
  - Cogwheel pursuits/saccadic intrusions
  - Hypokinesia
  - Bradykinesia
- Convergence insufficiency
  - May improve with dopaminergic therapy
    - Dopamine deficiency in basal ganglia? Vs. extranigral pathology
  - Prism
  - Convergence exercises (Lepore)
- Up-gaze limitation (but not a vertical gaze palsy)
- Ocular tremor
- Diplopia increases with disease progression, more common in patients with pre-existing phoria/tropia and daytime somnolence

Ekker MS, Janssen S, Seppi K et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. *Parkinsonism and Related Disorders*. 2017;42:1-10.
F.E. Lepore, Parkinson's disease and diplopia, Neuro-Ophthalmology 30 (2006) 37e40
Jehangir N, Yu CY, Song J, et al. Slower saccadic reading in Parkinson's disease. PLoS One 2018; 13:e0191005.
29. Ouerfelli-Ethier J, Elsaeid B, Desgroseilliers J, et al. Antisaccades predict cognitive functions in older adults and patients with Parkinson's disease. PLoS One 2018; 13:e0207589.
30. Walton CC, O'Callaghan C, Hall JM, et al. Antisaccade errors reveal cognitive control deficits in Parkinson's disease with freezing of gait. J Neurol 2015; 262:2745–2754.

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Eye Movement	Parkinsons	PSP	MSA
Smooth pursuit	Reduced pursuit gain Square-wave jerks Saccadic intrusions	Macro-square wave jerks	"poor"
Saccades	Hypometric voluntary saccades (reduced accuracy gain, increased latencies) Normal reflexive saccades	Hypometric (velocity gain lag, prolonged latencies) *Vertical – curved trajectory – "round the houses" sign* *Horizontal develop later in the disease*	Hypometric (prolonged latencies)
Peak Eye Velocities		Reduced	Normal
Possible pathophysiology	Executive dysfunction and overall cerebrum atrophy	Midbrain atrophy	Ponteocerebellar volume loss
Other	Convergence Insufficiency	Supranuclear gaze palsy *(vertical)*	Dry eye Skew deviation Divergence insufficiency

Crotty GF, Chwalisz BK. Ocular motor manifestations of movement disorders. *Curr Opin Neuro-Oph*. 2019;30(6):443-448

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FEMs in Parkinsonian Subtypes

- Increased frequency and magnitude of square wave jerks in microsaccades
- Able to differentiate PSP from PD patients
  - PSP reduced vertical component of microsaccades compared to other parkinsonian-dementia syndromes
- Saccades can differentiate subtypes of disease
  - PD - normal speed, mild hypometria
  - CBD - normal speed, mildly hypsometric, increased latency
  - MSA - normal speed, mild hypometria
  - SCA - Hypermetric
  - PSP - slow vertical saccades

Otero-Millan J, Schneider R, Leigh RJ, Macknik SL, Martinez-Conde S (2013) Saccades during Attempted Fixation in Parkinsonian Disorders and RecessiveAtaxia: From Microsaccades to Square-Wave Jerks. PLoS ONE 8(3): e58535. doi:10.1371/journal.pone.0058535

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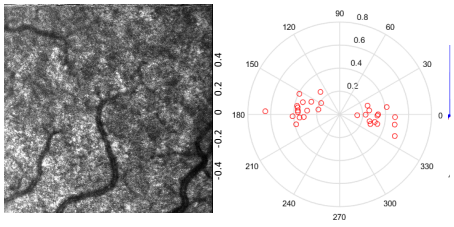
Abnormal FEMs

52 y/o Female,
complains of world "jittering" with fatigue,
nothing detected in clinic



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Case – 88 year old, Caucasian Female

- Chief Complaint: Intermittent horizontal diplopia at near
  - Been going on for 6 months
  - Occurs after 10-15 minutes of reading
  - Intermittent blur at near as well
- Pertinent medical history: Advanced Parkinson's disease
- Entering Visual Acuity cRx (Plano with +3.00 Add)
  - OD 20/25
  - OS 20/25
  - No improvement with pinhole

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Case – 88 year old, Caucasian Female

- Pertinent Exam Findings
  - Ocular posture: Exophoria – convergence insufficiency type
    - Distance Cover Test: 2 XP
    - Near Cover Test: 10 XP
  - Fusional Convergence: reduced at near
    - Distance x/4/2
    - Near x/4/2
  - Proximal Convergence: gross reduction
    - NPC: 30/40 x 3
  - Eye Movements
    - Fixation: Steady, (-) nystagmus
    - Pursuits: smooth
    - Saccades: hypermetric horizontally
  - Ocular Health: Dry Eye
    - TBUT 2 sec, 2+ MGD OU
- Diagnosis: Parkinson's disease with oculomotor sequelae
- Management:
  - BI prism Readers - 4BI with +2.50 add (increase working distance)
  - Dry Eye Treatment
  - Line guide

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Diplopia and Convergence Insufficiency

- May improve with dopaminergic therapy
  - *Pathophysiological hypothesis:*
    - *Dopaminergic deficiency in basal ganglia*
    - *Extranigral pathology*
- Treatment options
  - BI Prism
  - Convergence exercises
  - Decrease near add

F.E. Lepore, Parkinson's disease and diplopia, Neuro-Ophthalmology 30 (2006) 37e40.
Z. Almer, K.S. Klein, L. Marsh, M. Gerstenhaber, M.X. Repka, Ocular motor and sensory function in Parkinson's disease, Ophthalmology 119 (2012) 178e182.
V. Biousse, B.C. Skibell, R.L. Watts, D.N. Loupe, C. Drews-Botsch, N.J. Newman, Ophthalmologic features of Parkinson's disease, Neurology 62 (2004) 177e180.

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Case – 60 year old, Asian Female

- Referred by Neurologist to "help rule out oculomotor findings to help confirm diagnosis of Parkinsons disease"
- Chief Complaint: Patient has none, but very nervous
- Entering visual acuity sRx
  - OD 20/20
  - OS 20/20
- Ocular Posture: within norms
  - Distance Cover Test: ortho
  - Near Cover Test: 2 XP
- Fusional Vergences: within norms
- Proximal Convergence: Abnormal, asymptomatic
  - NPC: 15/20
- Eye Movements
  - Fixation: stable (-) nystagmus
  - Pursuits: saccadic intrusions/cogwheel horizontally
  - Saccades: Hypermetric horizontally>Vertically
- Ocular Health: Normal

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Case – 60 year old, Asian Female

- Diagnosis: Oculomotor findings (convergence insufficiency, cogwheel pursuits, hypermetric saccades) consistent with Parkinsons disease
- Management: Co-manage with neurology
  - Ocular treatment not necessary at this time as patient is asymptomatic
  - Offer pencil pushups

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Case – 80 year old, Caucasian Male

- Prism evaluation requested by neurology
- Chief complaint: intermittent horizontal diplopia at near when reading
  - Occurs after few mins reading with current bifocals
  - Denies diplopia at distance
- Pertinent Medical History: hyperlipidemia, hypothyroid, Parkinsons variant, mild cognitive impairment, atherosclerosis, dysphagia
  - Meds: Neurontin, levothyroid, cymbalta
- Personal Ocular History: retinal tear OS, PCIOL OU, trichiasis with lower lid entropion repair
  - Last eye exam with OPH 1 month prior

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Case – 80 year old, Caucasian Male

- Pertinent Exam Findings
  - Ocular Posture
    - Distance Cover Test: 0-2 EP
    - Near Cover Test: 0-4XP
  - Fusional Vergence
    - Distance Divergence: x/4/2, Convergence x/12/10
    - Near Divergence: x/14/12, Convergence x/4/0
  - Proximal Convergence: Reduced with fatigue component
    - NPC 20,23,24,26
- Eye movements: microsaccadic bursts on fixation
- Refraction
  - OD -0.50+2.00x010 20/30+
  - OS -2.25+3.00x005 20/25-2
  - Add +2.50
- Diagnosis: Parkinsons disease with convergence insufficiency
- Management: Single vision prism glasses
  - +2.00+2.00x010 2.5BI
  - +0.25+3.00x005 2.5BI
  - Backed off near add to increase working distance

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Case – 87 year old, Caucasian male

- Chief Complaint: intermittent horizontal diplopia – words move on the page with his new reading glasses
- Personal Medical History: Coronary artery disease, hypertension, atrial fibrillation, anemia, hearing loss, DM2 wo retinopathy, Parkinsons disease, anxiety
- Personal Ocular History: PCIOL OU, myopia with RPE atrophy, blepharitis OU
- Current Glasses (Last exam 1 month ago)
  - OD -0.25+2.00x175 20/25- 3.0BO
  - OS: +0.50+1.50x165 20/40+3.0BO
  - Add +3.25

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Case - 87year old, Caucasian male

- Current Rx
  - OD -0.25+2.00x175 20/25-2 3.0BO
  - OS: +0.50+1.50x165 20/30-2 3.0BO
  - Add +3.25
- Pertinent Exam findings
  - Ocular Posture *Comitant
    - Distance Cover Test cPrism (6BO): 4EP
    - Near Cover Test cPrism (6BO): 6XP
  - Fusional Vergences cPrism (6BO)
    - Distance Divergence x/-4/-2
    - Distance Convergence x/14/10
    - Near Divergence x/8/6 primary gaze, x/4/2 down gaze
    - Near Convergence x/6/4 primary gaze, x/1/0 down gaze
  - Proximal Convergence: reduced
    - NPC 17,19,20
- Diagnosis:
  - Parkinsons disease with convergence insufficiency
  - Distance Esophoria (longstanding)
  - Blepharitis, DM2 wo DR
- Final Trifocal
  - OD -0.25+2.00x170 5.0BO
  - OS: -0.25+1.50x165 5.0BO
  - Add +3.00
  - Trifocal – decenter lenses to induce BI prism
- Final Single vision near (no prism)
  - OD +2.75+2.00x170
  - OS: +2.75+1.50x165

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Case - 87year old, Caucasian male

- Diagnosis:
  - Parkinsons disease with convergence insufficiency
  - Distance Esophoria (longstanding)
  - Blepharitis, DM2 wo DR
- Final Trifocal
  - OD -0.25+2.00x170 5.0BO
  - OS: -0.25+1.50x165 5.0BO
  - Add +3.00
  - Trifocal – decenter lenses to induce BI prism
- Final Single vision near (no prism)
  - OD +2.75+2.00x170
  - OS: +2.75+1.50x165

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Case – 67 year old, Caucasian Male

- Chief Complaint: Reading is difficult
  - No blur/diplopia just difficult
  - Likes to read the newspaper and his kindle, brought it with him
- Pertinent medical history: moderate Parkinson's disease
- Pertinent exam findings
  - Visual Acuity: 20/20 OD/OS
  - Ocular Health: PCIOL OU, otherwise normal OU
  - Ocular Posture: within norms (ortho at distance and near)
  - Eye Movements: hypometric saccades
  - DEM
    - Vertical: 23 seconds
    - Horizontal: 40 seconds, with line guide 25 seconds
- Are the oculomotor sequelae the cause of the patient's reading complaints?

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Case – 67 year old, Caucasian Male

- Chief Complaint: Reading is difficult
  - No blur/diplopia just difficult
  - Likes to read the newspaper and his kindle, brought it with him
- Pertinent medical history: moderate Parkinson's disease
- Pertinent exam findings
  - Visual Acuity: 20/20 OD/OS
  - Contrast Acuity: 20/50 OD/OS
  - MVPT/TVPS: Difficulties with visual figure ground (simultanagnosia)
- Diagnosis: Parkinsons disease with ocular/visual sequelae: hypometric saccades, reduced contrast sensitivity, visual simultanagnosia
- Management:
  - Line guide, double spacing, increase font size
  - Kindle options, lighting options, discussion about contrast

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Visual Perceptual Impairments in Parkinson's

Visual Hallucinations

Reduced Visuospatial Perception
- Difficulties with line orientation
- Visualization of rotation
- Reduced depth perception
- Spatial working memory
- Impairments in motion detection, human movement

Visual Crowding Difficulties
- Difficulties seeing things in visually complex figures/background

Reduced Facial Recognition

Associated with gait freezing and dementia

Pathophysiology
- Grey matter atrophy in temporal/parietal lobes
- Primary visual cortex

Clinically – bump into doorways or objects, driving, navigating

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Visual Hallucinations and Parkinson's

- Prevalance ranges 4-83%
  - Most common "non-declared" symptom – often not reported spontaneously by the patient themselves, must be asked directly by the provider
- Definition
  - Perception of object/event in absence of external stimulus
  - Visual illusion
  - Passage of shadows
- Occurs earlier in Lewy-body Parkinsons (PD with dementia)
- Important predictors for development of dementia
- Once they exist, they persist and progress unless treated
- Associated with reduced VA, disease duration, reduced contrast sensitivity and color vision
- Can be triggered by dopaminergic and anticholinergic drugs
- You have to ask!

Ekker MS, Janssen S, Seppi K, et al. Ocular and visual disorders in Parkinson's disease: common but frequently overlooked. *Parkinsonism and Related Disorders.* 2017;40:1-10.

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Ocular and Visual disorders in Parkinson's

- Some result from neurodegenerative process of Parkinsons – and often respond to dopaminergic medication
- Others may be side effects of dopaminergic, cholinergic or nonadrenergic medication, and surgical interventions – deep brain stimulation and pallidotomy

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Ocular side effects of Parkinson's Medications

- Levodopa
  - Ocular dyskinesias, eyelid melanoma, mydriasis, lid ptosis, blepharospasm
  - Normalization of retinal dopamine may improve retina/contrast sensitivity, improve smooth pursuit and increase blink rate
- Cabergoline
  - Reduced contrast sensitivity
- Bromocriptine/dopamine agonists
  - Visual hallucination exacerbation
- Amantadine
  - Corneal endothelial dysfunction, punctate keratitis, mydriasis, reduced accommodation, blurred vision, visual hallucinations
- Benzhexol
  - Mydriasis, increased angle closure risk, photophobia, reduced accommodation, dry eyes, anisocoria, blurred vision
- MAO-B inhibitors
  - Blurred vision
- Dopamine-blocking agents
  - Oculogyric crises
- Imipramine
  - Mydriasis, cycloplegia, dry eyes, ocular muscle paresis, nystagmus
- Apomorphine
  - Improve contrast sensitivity and smooth pursuits

Ekker MS, Janssen S, Seppi K et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. *Parkinsonism and Related Disorders.* 2017;40:1-10.

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Ocular/visual side effects of Deep brain stimulation (DBS)

Nucleus subthalamicus
- Visual hallucinations
- Vertical diplopia 2/2 skew deviation
- Contraversive eye deviation
- Reduced voluntary ipsilateral gaze
- Eyelid apraxia
- Involuntary eyelid closure
- Fixation instability
- Torsional nystagmus
- Unilateral mydriasis

Nucleus pedunculopontine
- oscillopsia

Ekker MS, Janssen S, Seppi K et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. *Parkinsonism and Related Disorders.* 2017;40:1-10.

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Thank you!
Questions?

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