

NEURODEGENERATIVE DISEASE IN OPTOMETRIC PRACTICE

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Financial Disclosures

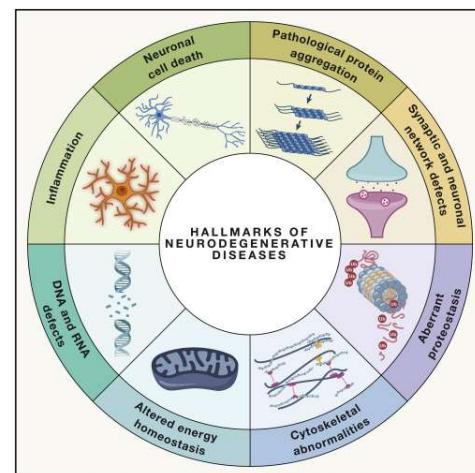
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Objectives

- Provide a brief overview of the pathophysiology of Parkinson's and Alzheimer's disease.
- Review common systemic findings in both neurodegenerative conditions with an emphasis on early clinical manifestations.
- Utilize case reports to not only review common ocular manifestations of Parkinson's and Alzheimer's, but to also increase the primary care optometrist's confidence in managing these patients.

Neurodegenerative Disease

- Characterized by **progressive loss** of neurons, typically affecting groups of neurons with **functional interconnections**
- Most common distinct feature → **protein aggregate accumulation**



Source: Wilson, D. M., 3rd, Cookson, M. R., Van Den Bosch, L., Zetterberg, H., Holtzman, D. M., & Dewachter, I. (2023). Hallmarks of neurodegenerative diseases. *Cell*, 186(4), 693–714. <https://doi.org/10.1016/j.cell.2022.12.032>

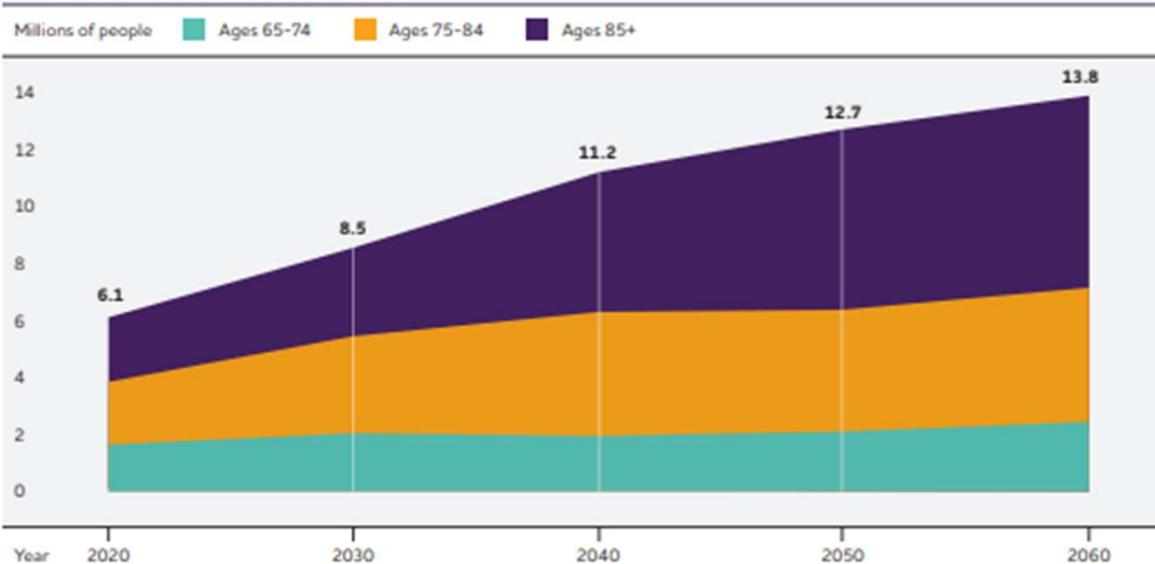
Major Neurodegenerative Disease



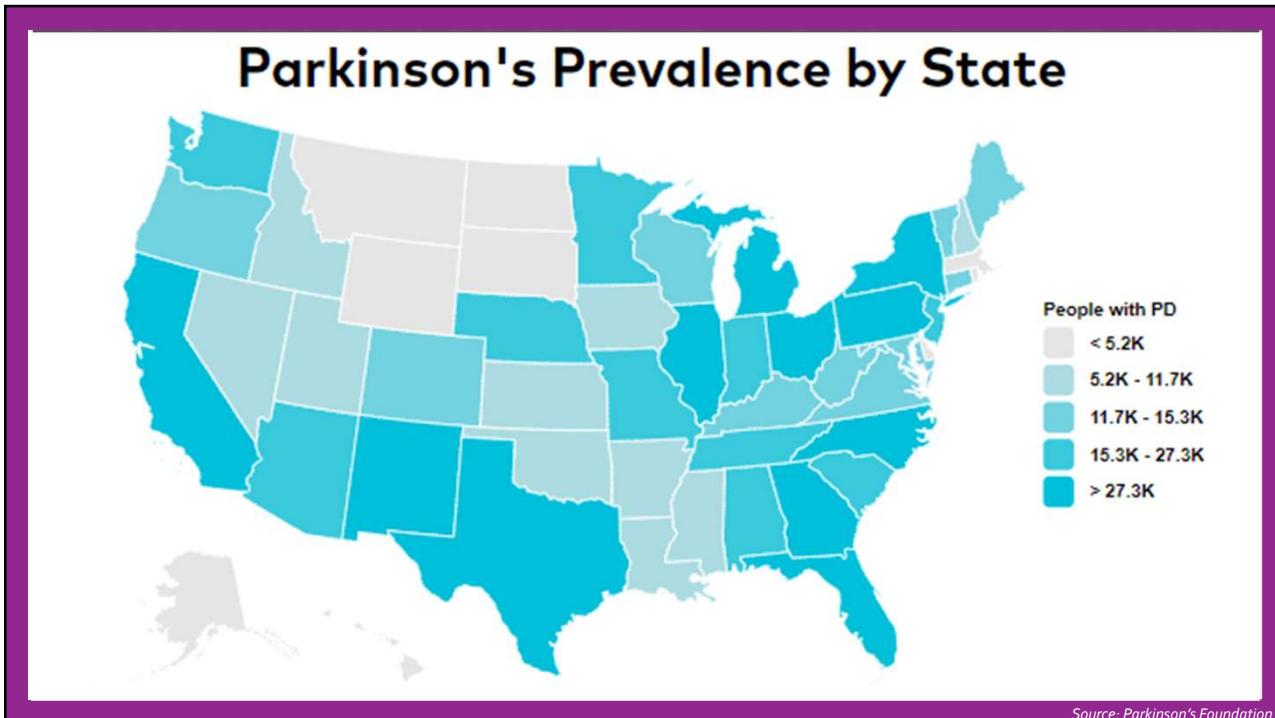
Disease	Clinical Pattern	Protein Inclusions
Alzheimer disease (AD)	Dementia	A β (plaques) Tau (tangles)
Frontotemporal lobar degeneration (FTLD)	Behavioral changes, language disturbance	Tau TDP43 Others (rare)
Parkinson disease (PD)	Hypokinetic movement disorder	α -synuclein Tau
Huntington disease (HD)	Hyperkinetic movement disorder	Huntingtin (polyglutamine repeat expansions)
Spinocerebellar ataxias	Cerebellar ataxia	Various proteins (polyglutamine repeat expansions)
Amyotrophic lateral sclerosis (ALS)	Weakness with upper and lower motor neurons signs	SOD1 TDP43

Source: Kumar, V., Abbas, A. K., & Aster, J. C. (2017). *Robbins Basic Pathology* (10th ed.). Elsevier - Health Sciences Division.

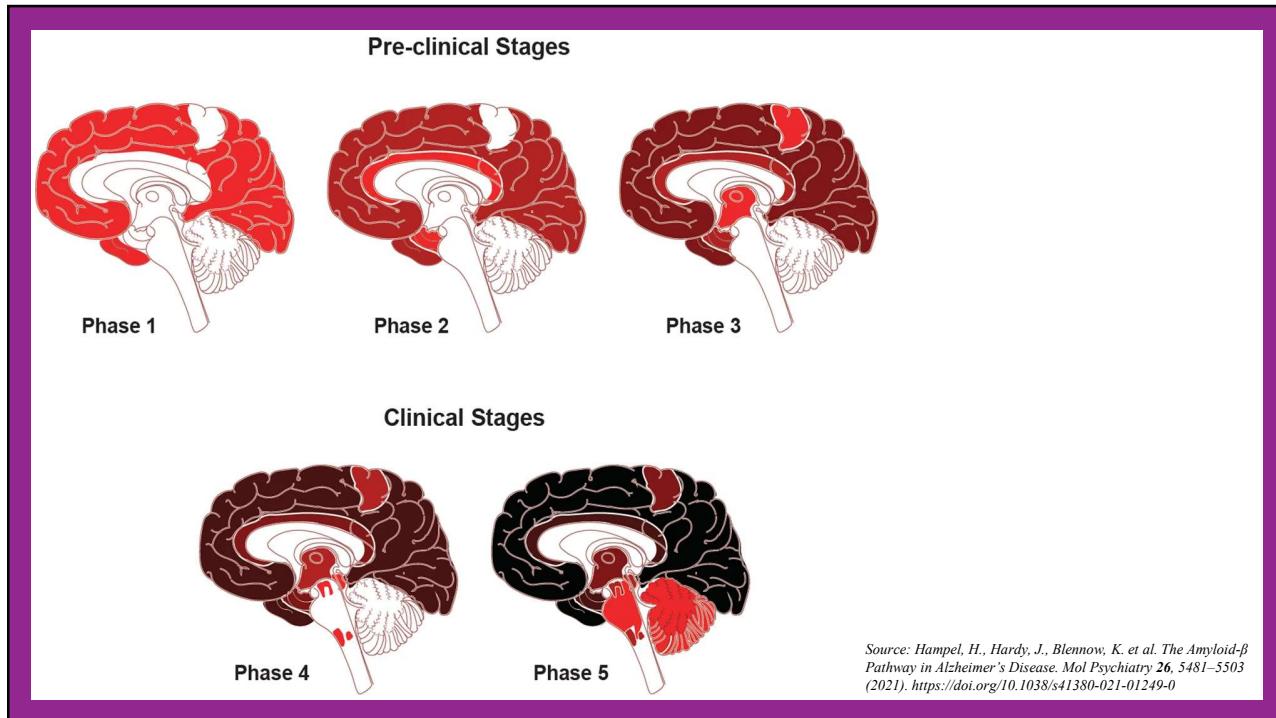
Projected Number of People Age 65 and Older (Total and by Age) in the U.S. Population with Alzheimer's Dementia, 2020 to 2060



Source: Alzheimer's Foundation

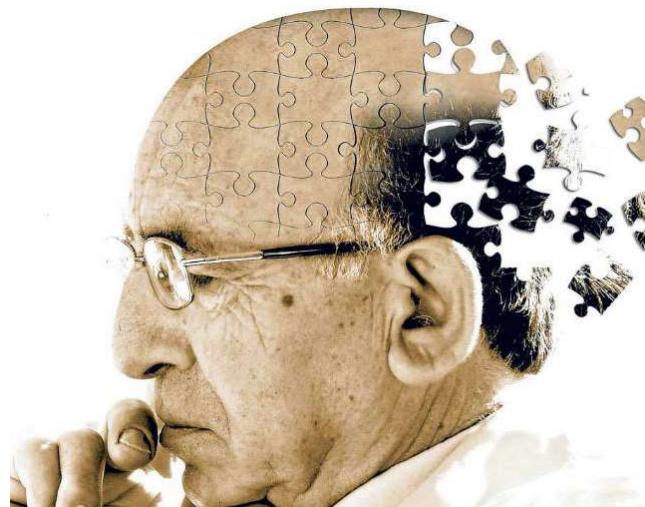


ALZHEIMER'S DISEASE



5 A's of Alzheimer's

- Agnosia
- Amnesia
- Anomia
- Aphasia
- Apraxia

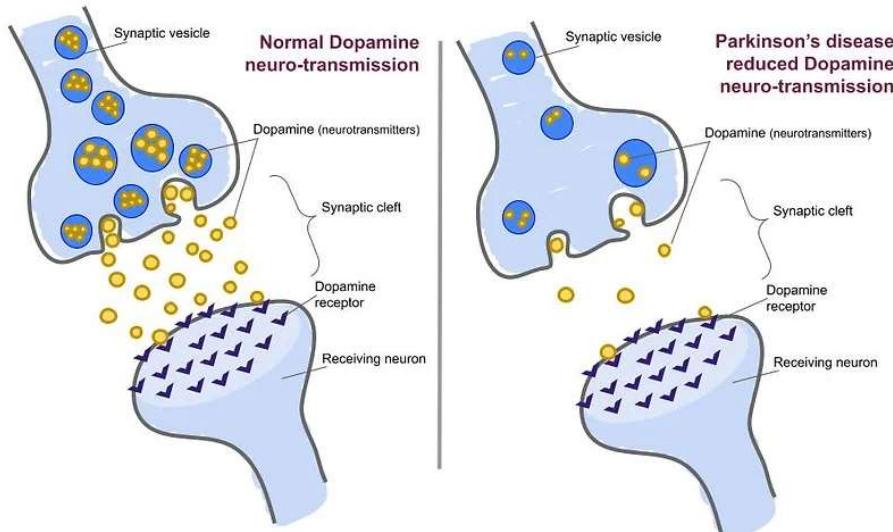


Additional Systemic Characteristics of Parkinson's

- Disturbance in Executive Functioning
 - Planning
 - Organizing
 - Sequencing
 - Abstraction
 - Judgement
- Impairment in Social and Occupational Function

PARKINSON'S DISEASE

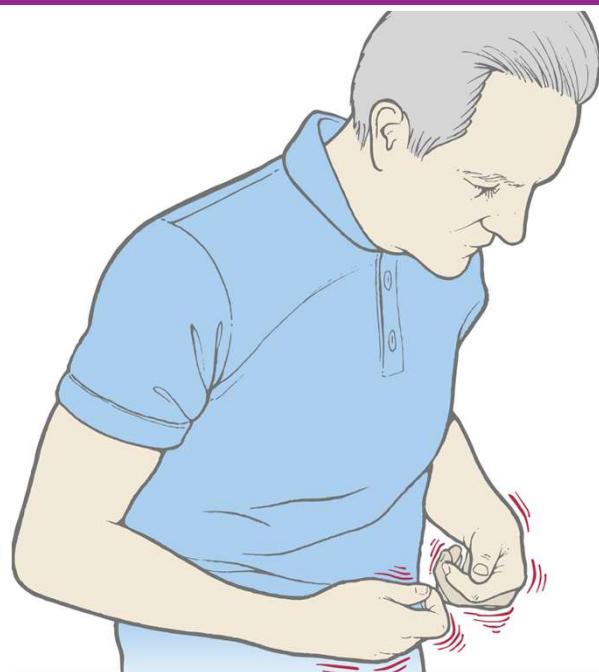
Parkinson's Disease



Source: Pilates for Parkinson's

Classic Picture of Parkinson's Disease

- Pill-rolling tremor
- Blank stare
- Flexed posture
- Paucity of movement



Additional Systemic Characteristics of Parkinson's

- High level cognitive dysfunction
- Language dysfunction
- Gait disturbance
 - i.e. shuffling gait
- Mood and behavioral problems
- Obsessive compulsive behaviors
- Decreased proprioception
- Orthostatic hypotension

Case Review Commonalities

- Each patient will have
 - Alzheimer's or Parkinson's
 - Chief complaint of "blurry vision"
 - History of bilateral cataract extraction

CASE #1

Case Report

- 76-year-old Caucasian male presents for second opinion re: progressives
 - Intermittent
 - Worse at end of day
 - (+)photosensitivity



Medical History	Medications
Depression Parkinson's Hypertension Hypercholesterolemia Type II Diabetes Mellitus	Zoloft Amantadine Amlodipine Atorvastatin Metformin

Pertinent Entrance Exam Findings

- DVAcc: 20/40 OD/OS – Snellen High Contrast
- NVAcc: 20/70 OD/OS – Isolated Snellen 20/80 OU -- Continuous text
- EOMs: Truncated OU
- Saccades: Hypermetric OU
- Fixation: Compromised OU

Pertinent Trial Frame Findings

- No refractive change found
- DVAs in DVO Trial Frame:
 - 20/30+ OD/OS w/ Snellen High Contrast
- NVAs in NVO Trial Frame:
 - 20/40 OD/OS with isolated Snellen
 - Difficult 20/40 OU with continuous text



Ophthalmologic features of Parkinson's disease

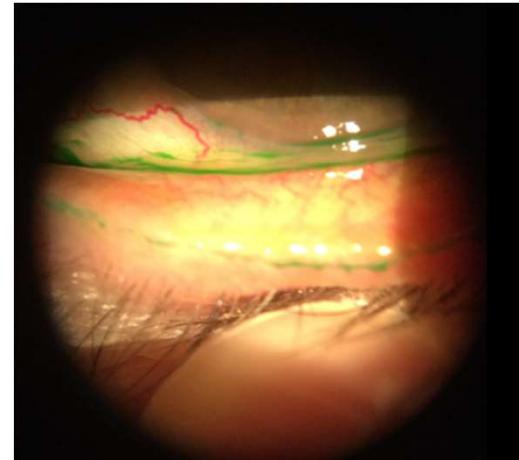
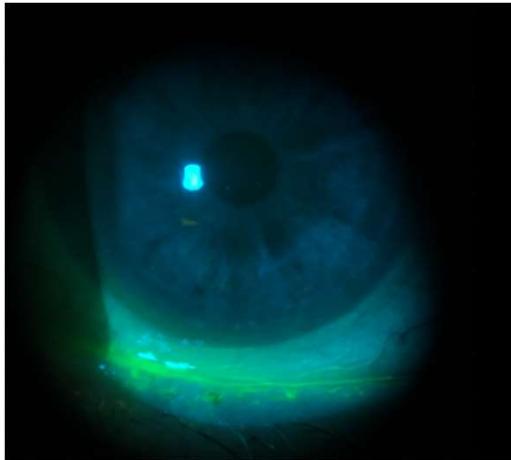
Refractive prescribing considerations include:

- Avoidance of bifocals and progressives
- Consider impact resistant material for lenses
- Reduce astigmatism by its spherical equivalent



Source: Bioussse, V., Skibell, B. C., Watts, R. L., Loupe, D. N., Drews-Botsch, C., & Newman, N. J. (2004). Ophthalmologic features of Parkinson's disease. Neurology, 62(2), 177–180. <https://doi.org/10.1212/01.wnl.0000103444.45882.d8>

Pertinent Slit Lamp Findings



No corneal edema OU

Prevalence and characteristics of dry eye disease in Parkinson's disease: a systematic review and meta-analysis

Presenting in **61.1%** of Parkinson patients
Pertinent test findings include **decreased**:

- Blink rate
- Corneal thickness
- TFBUT
- Tear secretion

Increased incidence of *S. aureus* and *Corynebacterium*

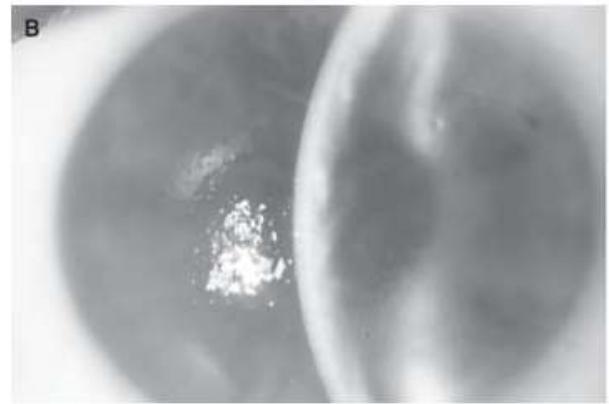
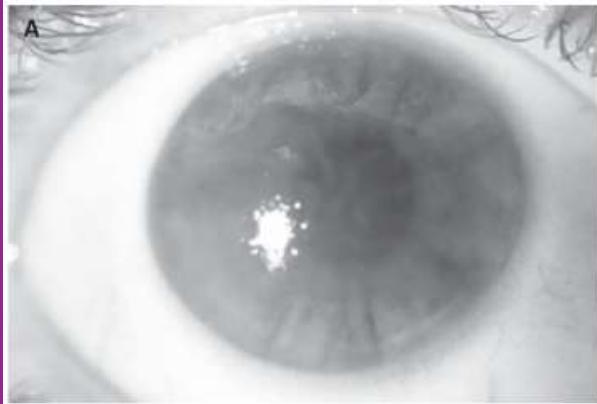
- Seborrheic dermatitis
- Oily skin
- Meibomitis

Source: Nagino, K., Sung, J., Oyama, G., Hayano, M., Hattori, N., Okumura, Y., Fujio, K., Akasaki, Y., Huang, T., Midorikawa-Inomata, A., Fujimoto, K., Eguchi, A., Hiramatsu, S., Miura, M., Ohno, M., Hirose, K., Morooka, Y., Murakami, A., Kobayashi, H., & Inomata, T. (2022). Prevalence and characteristics of dry eye disease in Parkinson's disease: a systematic review and meta-analysis. *Scientific reports*, 12(1), 18348. <https://doi.org/10.1038/s41598-022-22037-y>



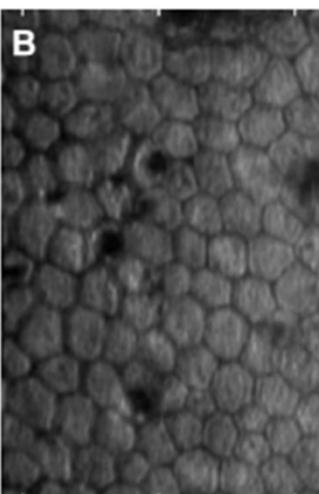
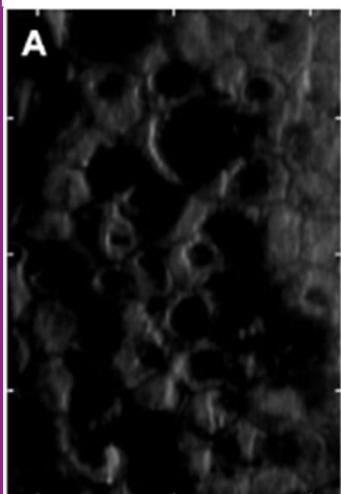
Bilateral Reversible Corneal Edema Associated With Amantadine Use

[Salomon Esquenazi](#)



Common **reversible** side effect
Presents weeks to months following drug initiation
More common if dosage is 200+mg/day

Clinical and genetic investigation of amantadine-associated corneal edema



Does amantadine cause irreversible endothelial loss OR does it accelerate progression of endothelial loss?

Source: Hessen, M. M., Vahedi, S., Khoo, C. T., Vakili, G., & Eghrari, A. O. (2018). Clinical and genetic investigation of amantadine-associated corneal edema. *Clinical ophthalmology (Auckland, N.Z.)*, 12, 1367–1371. <https://doi.org/10.2147/OPTH.S166384>

Pertinent Low Vision Findings

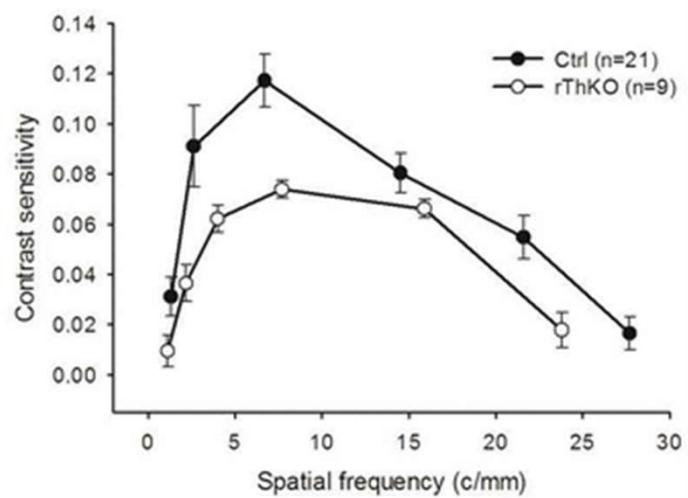
- Farnsworth D-15
 - Normal color vision OU
- Contrast Sensitivity with Mars:
 - 1.20 OU
 - Moderate loss



The influence of dopamine on contrast sensitivity in physiologically defined retinal ganglion cells

Michael L Risner; David Sprinzen; Douglas McMahon

Confirmed that light-mediated vision such as contrast sensitivity is negatively altered in mice models lacking retinal dopamine



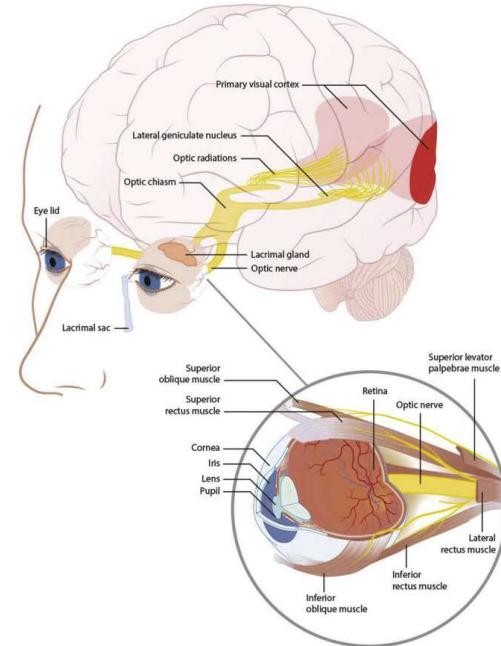
Case 1 Clinical Pearls

- Recommend the following:
 - NVO/DVO glasses with impact resistant lenses
 - Reading stand
 - Filters
- Consider anterior segment implications
 - Gel tears w/ drop guide
 - Meibomian gland and blepharitis consideration
 - Large frames
- Rule out corneal edema for those on amantadine
 - Assess corneal endothelium

CASE 2

Case History

- 73-year-old Caucasian male complains of blurred vision OU
 - Near>Distance
 - Onset: 3 months ago
 - Associated symptom of **diplopia** at near
 - ~70% of time



Medical History

Depression
Parkinson's
Hypertension
Cardiovascular disease
Benign prostate hypertrophy
Environmental allergies

Medications

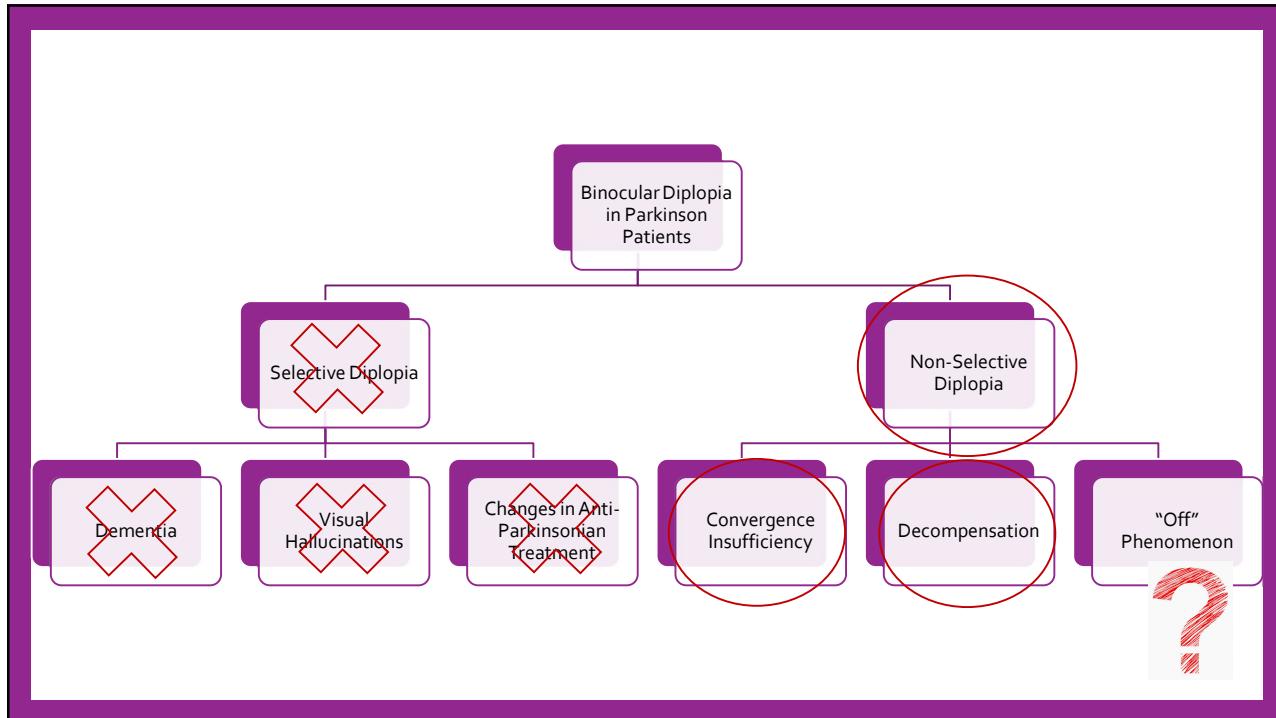
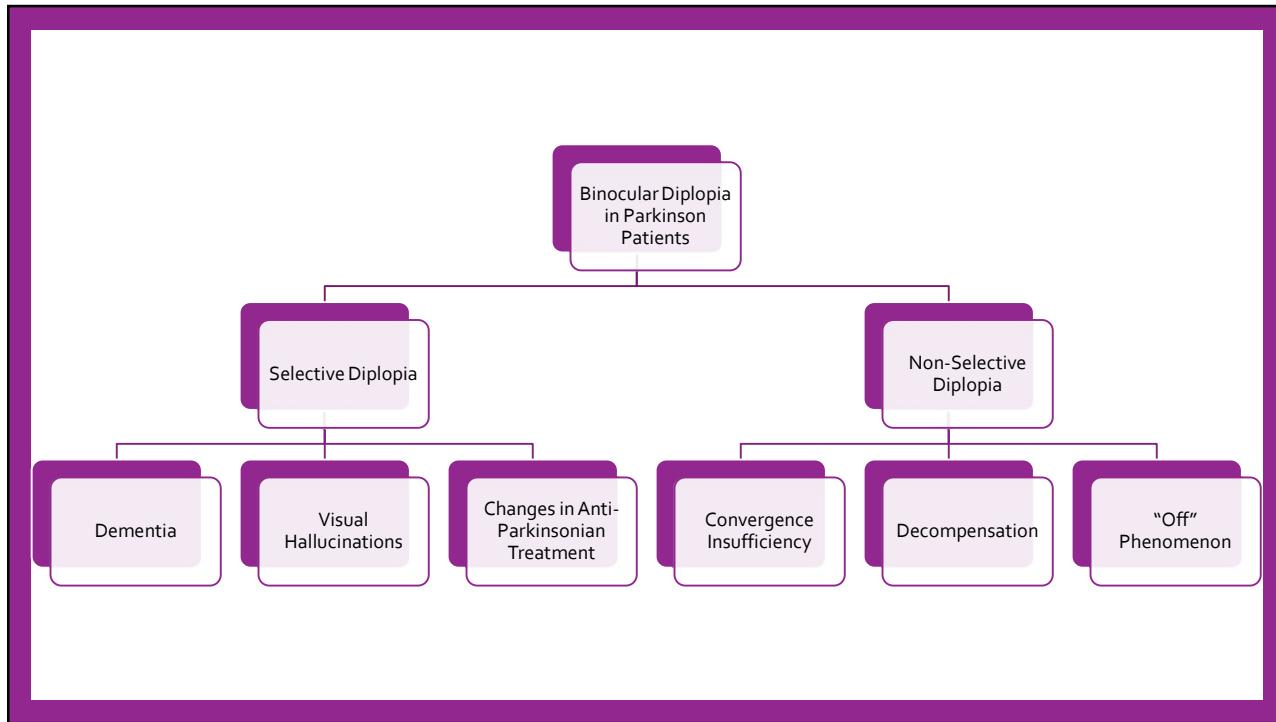
Effexor
Carbidopa 25 / Levodopa 100
Metoprolol succinate
HCTZ/Losartan K+
Eliquis
Tamsulosin
Claritin

Pertinent Entrance Exam Findings

- DVAcc: 20/30 OD/OS – Snellen High Contrast
- NVAcc: 20/30 OD/OS – Isolated Snellen
 - Attempted continuous text OU – diplopia noted
- EOMs: Truncated OU
- Saccades: Hypermetric OU
- Fixation: Compromised OU

**NO CHANGE IN RX
DURING REFRACTION...**

Onto diplopia work-up



Pertinent Binocular Vision Findings

- DCTcc: 2xp
- NCTcc: 12xp'
- NPC (cm): 17 cm
- PFV: x/4/2

- **Diagnosis of Convergence Insufficiency**
 - Compensating prism?
 - Vision therapy?



Orthoptic Treatment of Convergence Insufficiency in Parkinson's Disease: A Case Series

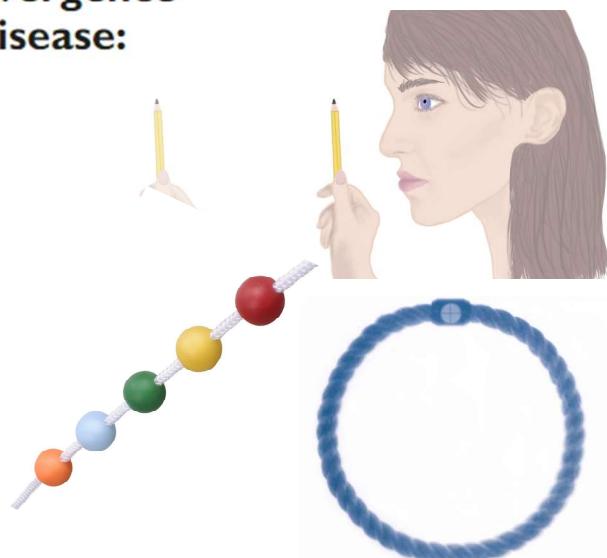
25 patients considered for study

7 agreed to undergo treatment

2/7 completed treatment
Noticed decreased signs and symptoms

5/7 abandoned treatment

- Fragility & fatigue 2' Parkinson's



Source: Kergoat, Hélène & Law, Caroline & Chriqui, Estefania & Kergoat, Marie-Jeanne & Leclerc, Bernard-Simon & Panisset, Michel & Postuma, Ronald & Irving, Elizabeth. (2017). Orthoptic Treatment of Convergence Insufficiency in Parkinson's Disease: A Case Series. *Cranio-Orbito-Neurofacial Medicine*, 12(1), 1-6.



Source: *Review of Optometry*

1 MONTH FOLLOW-UP

Pertinent Findings

- Decreased symptomology per patient
- Confirmation that Carbidopa 25 / Levodopa 100 is not impacting visual symptoms
- NCTcc: 6-8 XP'
- NPC (cm): 12.0
- PVF: x/10/10

LET'S PRESCRIBE!

Case 2 Clinical Pearls

- Selective vs. Non-Selective Diplopia
 - Selective → discuss with neurologist
 - Non-Selective
 - Treat binocular dysfunction
 - Consider "off" phenomenon
- Discuss vision therapy vs. compensating prism
 - Consider Fresnel before prescribing
 - Helps verify if non-selective diplopia is associated with "off" phenomenon

CASE 3

Case History

- 70-year-old Caucasian male complains of blurred vision OU
 - Near>Distance
 - Onset: 6 months ago
 - No relief with OTC readers
 - "Cataract surgery was a waste"



Medical History	Medications
Depression Hypertension Chronic obstruction Benign prostate hypertrophy Osteoarthritis Environmental allergies Functional dyspepsia	Fluoxetine Carbidopa 25 / Levodopa 100 Metoprolol succinate HCTZ/Losartan K+ Effexor Dexilant Ibuprofen Eliquis Tamsulosin Claritin

Orientation & Affect: agitated ; paranoid

Patients with Paranoid Symptoms: Considerations for the Optometrist

Most Common Associations:

- 1) Drug abuse
- 2) Neurodegenerative diseases
- 3) Mental health conditions
 - Schizophreniform disorder
 - Schizoaffective disorder
 - Paranoid personality disorder



Source: Bampton, Mark & Neiberg Maryke N (2013). Patients with Paranoid Symptoms: Considerations for the Optometrist. *Optometry & Visual Performance*, 3, 1.

Patients with Paranoid Symptoms: Considerations for the Optometrist

Challenge: establish a working alliance in few visits while simultaneously gaining **some** patient trust.

Consider the following mnemonic

C onfidentiality
H umor
Explain
M otive



Source: Bampton, Mark & Neiberg Maryke N (2013). Patients with Paranoid Symptoms: Considerations for the Optometrist. *Optometry & Visual Performance*, 3, 1.

Confidentiality

- Reiterate laws of patient confidentiality **directly**
 - Do not have tech or front desk staff complete this
- Acknowledge that patient is wise by being protective of personal and/or medical information



Source: Bampton, Mark & Neiberg Maryke N (2013). Patients with Paranoid Symptoms: Considerations for the Optometrist. *Optometry & Visual Performance*, 3, 1.

Humor

- Utilize if things get tense
- **NEVER** allow patient to feel teased or ridiculed
 - Laugh at yourself
 - Reference popular movies



Source: Bampton, Mark & Neiberg Maryke N (2013). *Patients with Paranoid Symptoms: Considerations for the Optometrist*. *Optometry & Visual Performance*, 3, 1.

Explain

- Provide **purpose** and/or function of every test during exam process
 - Preface with "*this is part of the routine examination that we do for all our patients*"



Source: Bampton, Mark & Neiberg Maryke N (2013). *Patients with Paranoid Symptoms: Considerations for the Optometrist*. *Optometry & Visual Performance*, 3, 1.

Motivation

- Assure patient that participation in examination process is entirely voluntary

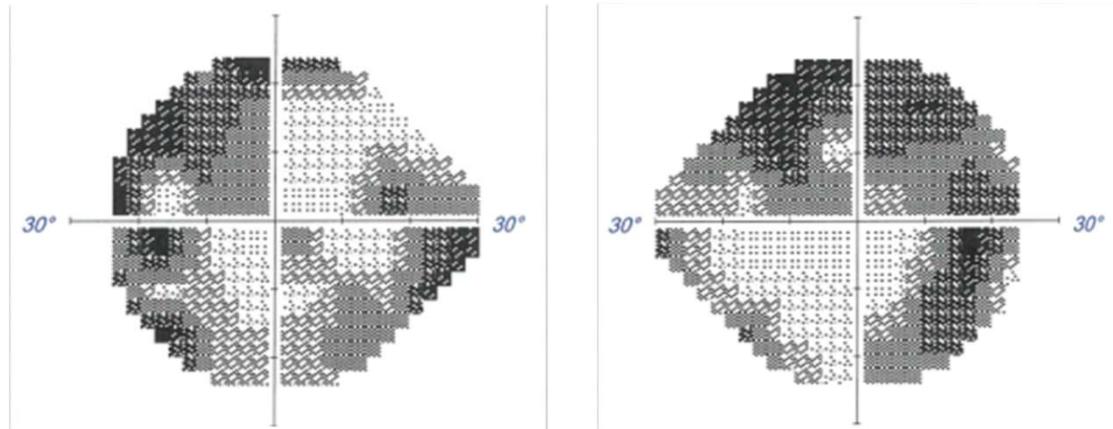


Source: Bampton, Mark & Neiberg Maryke N (2013). *Patients with Paranoid Symptoms: Considerations for the Optometrist*. *Optometry & Visual Performance*, 3, 1.

Pertinent Entrance Exam Findings

- DVAsc: 20/40 OD/OS with Snellen Acuity ; BCVA: 20/30 OD/OS
- NVAsc: 20/100 OU with Isolated Snellen ; BCVA: 20/30 OU
- EOMs: SAFE OU
- Pupils: PERRL (-APD)
- CVF: Restricted 360° OD/OS
 - Difficulty comprehending?
 - Compromised peripheral vision?

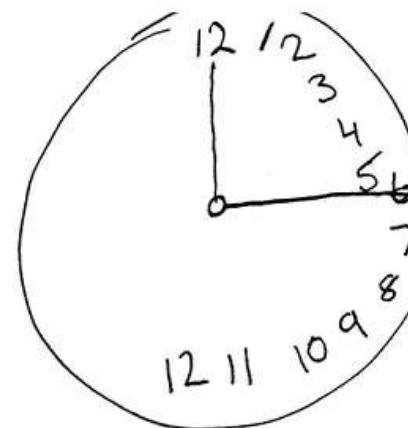
Automated Visual Fields



The Clock Drawing Test: A review of its accuracy in screening for dementia

Assesses the following cognitive skills:

- Short term memory
- Understanding verbal instructions
- Spatial orientation
- Abstract thinking
- Planning
- Concentration
- Executive skills
- Visuospatial skills



Source: Aprahamian I, Martinelli JE, Neri AL, Yassuda MS. The Clock Drawing Test: A review of its accuracy in screening for dementia. Dement Neuropsychol. 2009 Apr-Jun;3(2):74-81. doi: 10.1593/S1980-57642009DN30200002. PMID: 29213615; PMCID: PMC6666777.

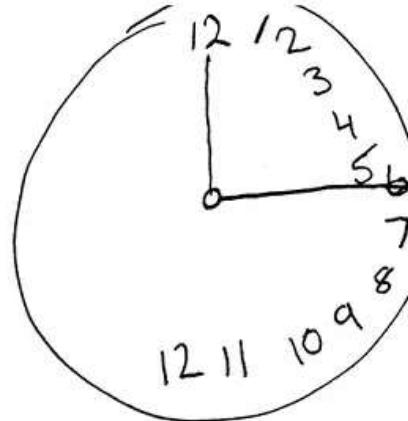
The Clock Drawing Test: A review of its accuracy in screening for dementia

Conclusions:

Accurately discriminates cognitively unimpaired patients from those showing early cognitive decline

High correlation between test and longer screeners such as MMSE and SKT

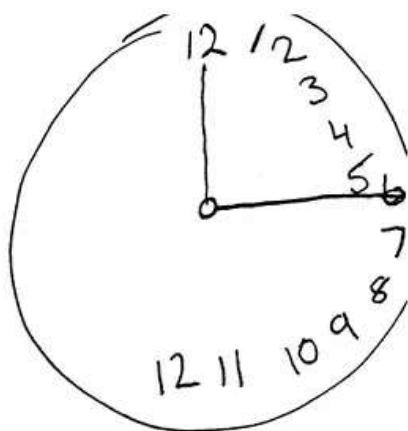
May provide more comprehensive cognitive examination in those with suspected early dementia states (i.e. visuospatial function & executive function)



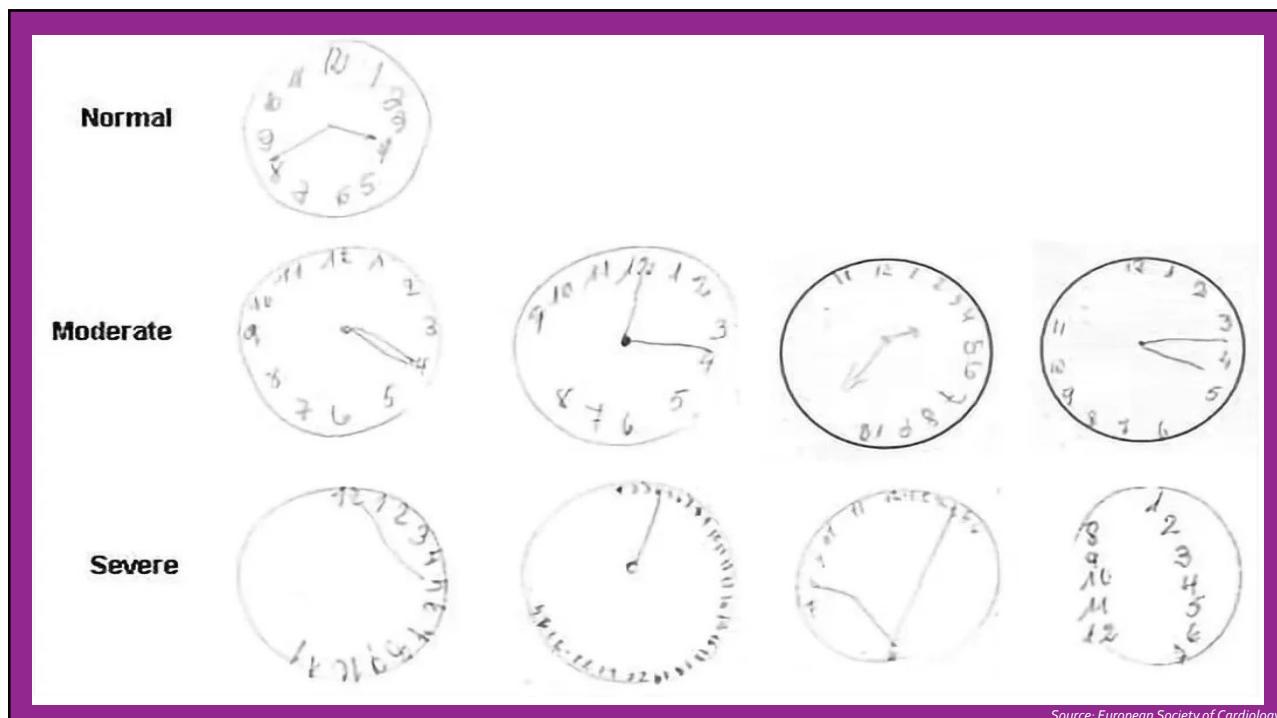
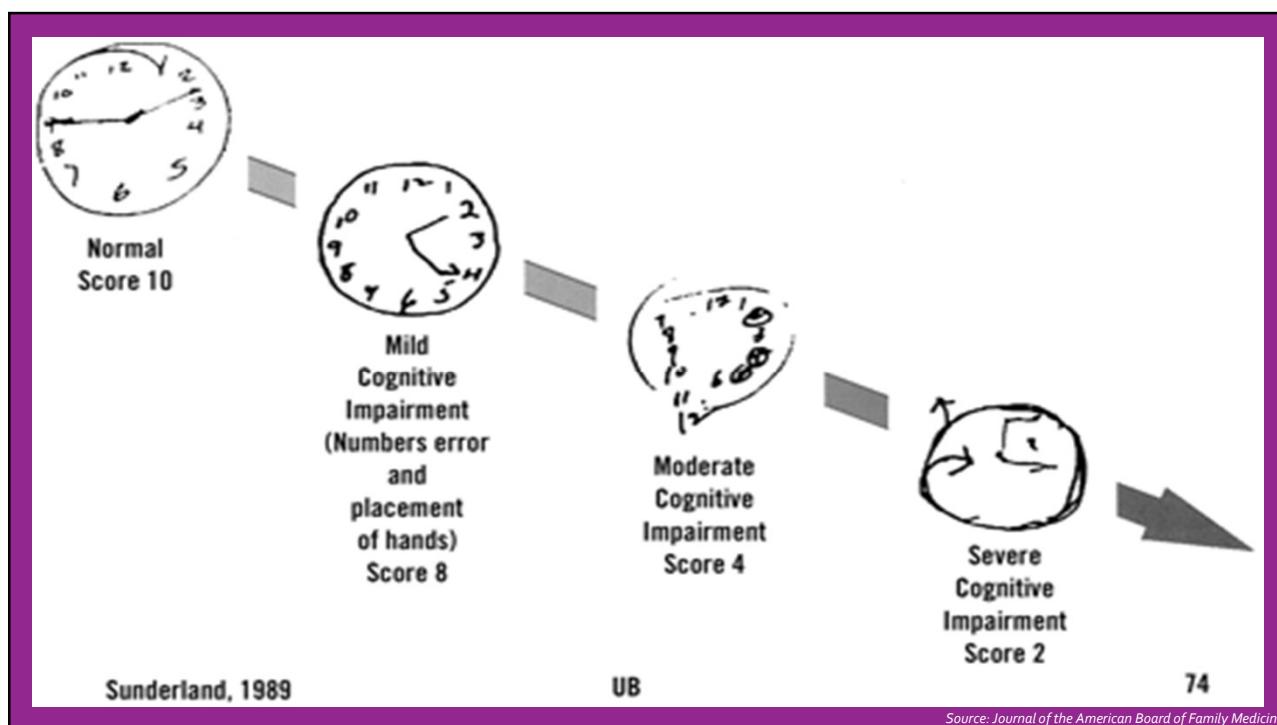
Source: Aprahamian I, Martinelli JE, Neri AL, Yassuda MS. The Clock Drawing Test: A review of its accuracy in screening for dementia. *Dement Neuropsychol*. 2009 Apr-Jun;3(2):74-81. doi: 10.1590/51980-57642009DN30200002. PMID: 29213615; PMCID: PMC6460922.

How To Administer the Clock Drawing Test

- Draw a circle on a blank piece of paper
 - Doctor vs. Patient
- Instruct them to place numbers on clock face
- Ask them to draw hands of clock to read specific time



Source: Aprahamian I, Martinelli JE, Neri AL, Yassuda MS. The Clock Drawing Test: A review of its accuracy in screening for dementia. *Dement Neuropsychol*. 2009 Apr-Jun;3(2):74-81. doi: 10.1590/51980-57642009DN30200002. PMID: 29213615; PMCID: PMC6460922.



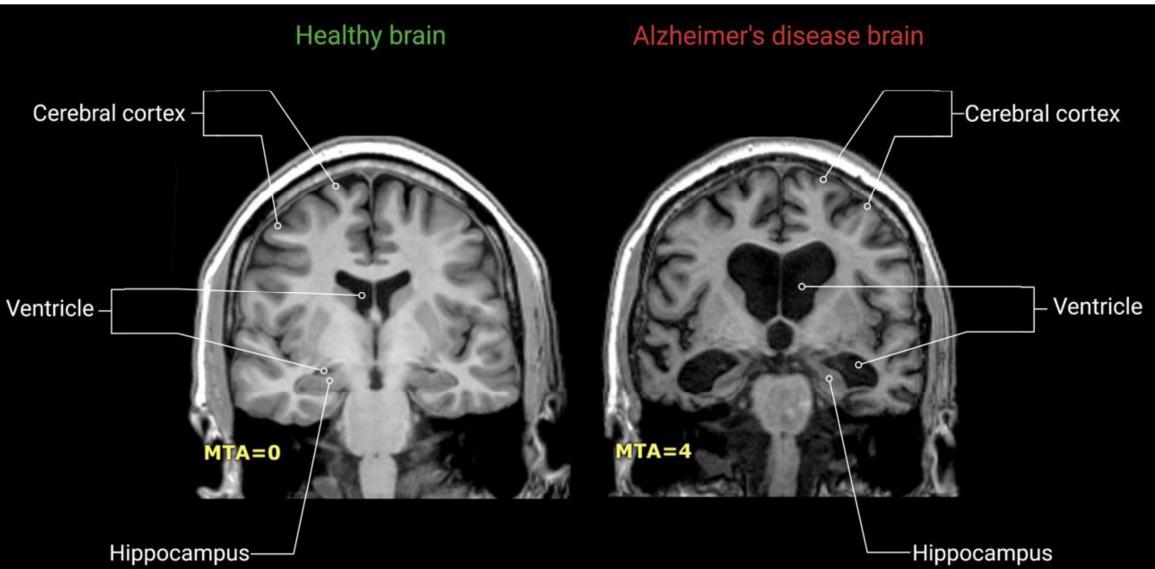
ANTERIOR SEGMENT

Unremarkable

POSTERIOR SEGMENT

Unremarkable

REFERRAL PLACED



Source: van Oostveen, W. M., & de Lange, E. C. M. (2021). Imaging Techniques in Alzheimer's Disease: A Review of Applications in Early Diagnosis and Longitudinal Monitoring. *International Journal of Molecular Sciences*, 22(4), 2110. MDPI AG. Retrieved from <http://dx.doi.org/10.3390/ijms22042110>

Case 3 Clinical Pearls

- Utilize mnemonic **CHEM** for any patient who presents with paranoid symptoms
- Consider testing **executive function**
 - Suspicious re: cognitive status
 - Tamper exam expectations
 - Changes in testing protocols
- Rule out **ocular disease** before classifying as *simply* neurodegenerative
- Interdisciplinary care is **common** with these patients

CASE 4

Case History

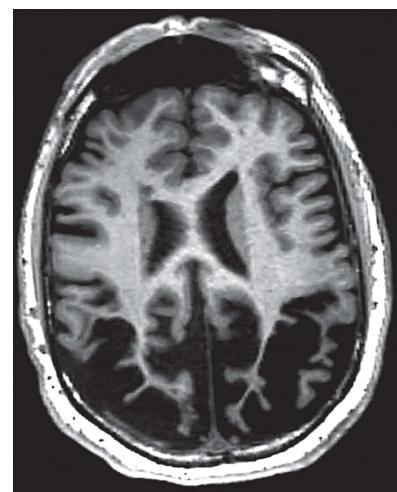
- 65-year-old Caucasian female presents to vision rehabilitation secondary to **Posterior Cortical Atrophy** with husband
 - Reduced
 - Vision near>distance
 - Color vision
 - Spatial awareness
 - Depth perception
 - **Goals:**
 - Reading
 - Distinguish food on plate
 - Increase mobility



Posterior Cortical Atrophy

- Rare, progressive neurodegenerative disease
- Characterized by
 - Neurodegeneration of **posterior cortical regions**
 - **Early visual dysfunction**
- Underlying causes include
 - Alzheimer's
 - *Visual variant*
 - Dementia with Lewy bodies
 - Creutzfeldt-Jakob disease

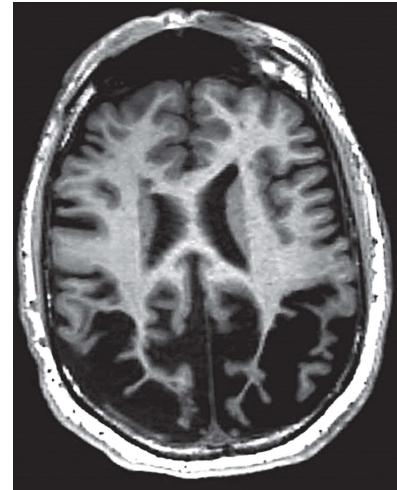
Source: Crutch, S. J., Schott, J. M., Rabinovici, G. D., Murray, M., Snowden, J. S., van der Flier, W. M., Dickerson, B. C., Vandenberghe, R., Ahmed, S., Bak, T. H., Boeve, B. F., Butler, C., Cappa, S. F., Ceccaldi, M., de Souza, L. C., Dubois, B., Felician, O., Galasko, D., Graff-Radford, J., Graff-Radford, N. R., ... Alzheimer's Association ISTAART Atypical Alzheimer's Disease and Associated Syndromes Professional Interest Area (2017). Consensus classification of posterior cortical atrophy. *Alzheimer's & dementia : the journal of the Alzheimer's Association*, 13(8), 870–884. <https://doi.org/10.1016/j.jalz.2017.01.014>



Posterior Cortical Atrophy

- Age of onset: mid-50s to early 60s
- Initial presentation → loss of higher visual function
 - Reduced visual fields
 - Diminished color vision
 - Difficulty with contour integration
 - Diminished ability to interpret, locate or reach for objects under visual guidance
- End stage: diffuse pattern of cognitive dysfunction

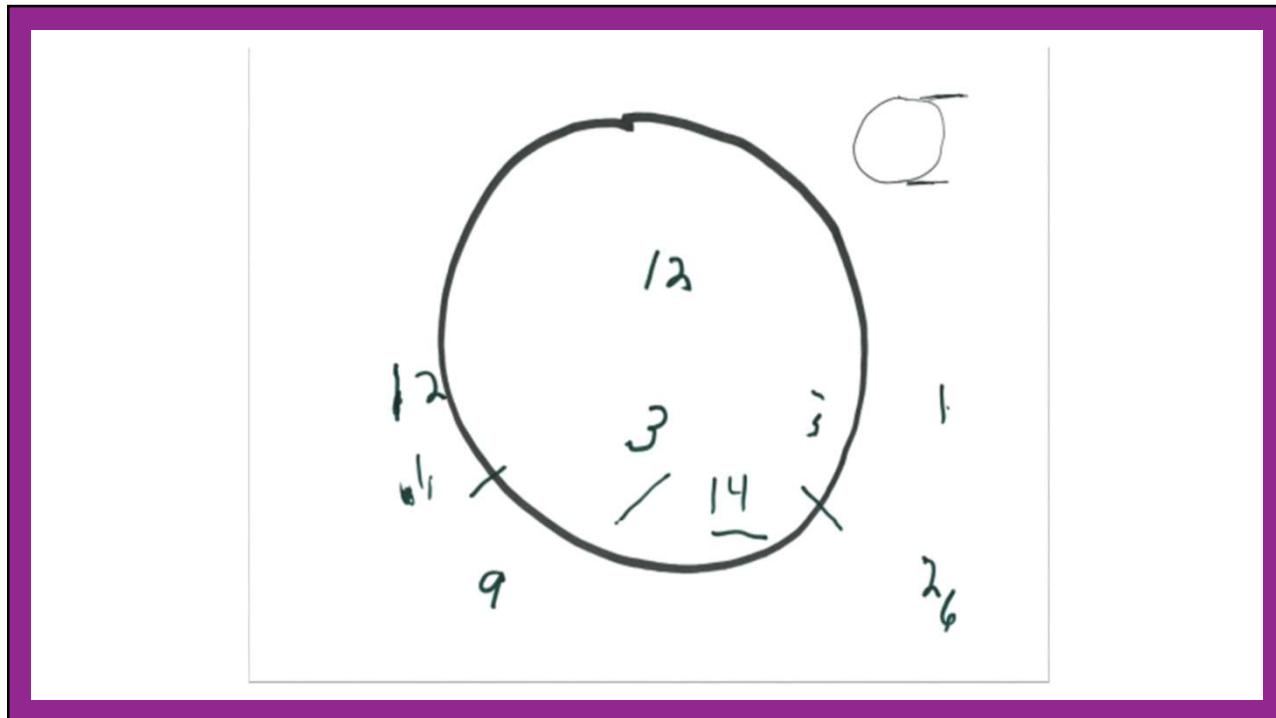
Source: Crutch, S. J., Schott, J. M., Rabinovici, G. D., Murray, M., Snowden, J. S., van der Flier, W. M., Dickerson, B. C., Vandenberghe, R., Ahmed, S., Bak, T. H., Boeve, B. F., Butler, C., Cappa, S. F., Ceccaldi, M., de Souza, L. C., Dubois, B., Felician, O., Galasko, D., Graff-Radford, J., Graff-Radford, N. R., ... Alzheimer's Association ISTAART Atypical Alzheimer's Disease and Associated Syndromes Professional Interest Area (2017). Consensus classification of posterior cortical atrophy. *Alzheimer's & dementia: the journal of the Alzheimer's Association*, 13(8), 870–884. <https://doi.org/10.1016/j.jalz.2017.01.014>



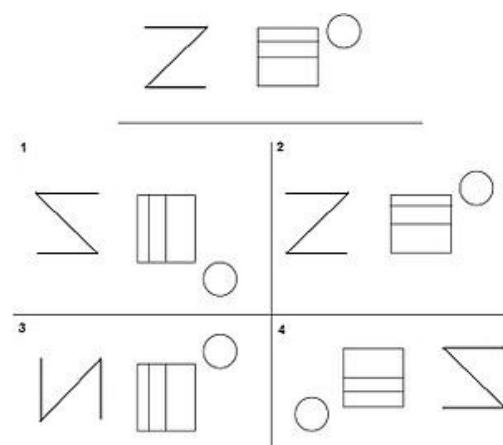
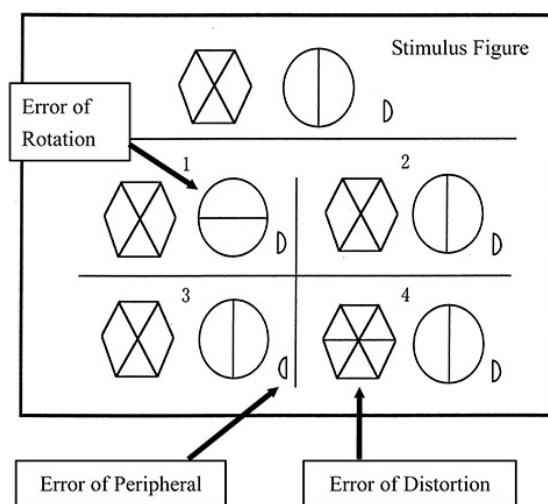
Screening Tests for Posterior Cortical Atrophy

- Utilized to differentiate between basic visual difficulties versus posterior cortical atrophy
 - Clock Drawing
 - Simple
 - Indicative of disordered visuospatial relationships
 - Benton Form Discrimination Test
 - Three form identification tests
 - Four visuo-spatial tests
 - Lower scores in PCA patients vs. normal controls

Source: Trobe JD, Butter CM. A screening test for integrative visual dysfunction in Alzheimer's disease. *Arch Ophthalmol* 1993;111:815-18.

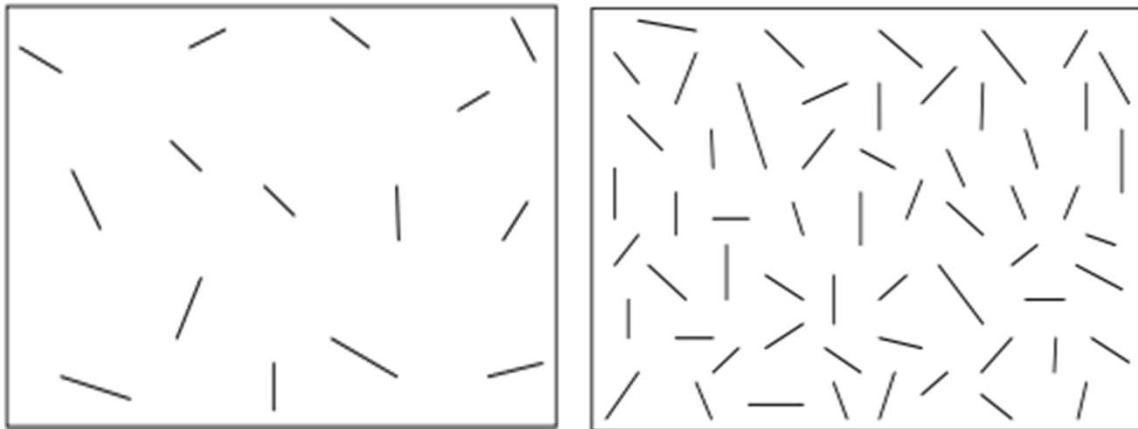


Benton Form Discrimination Test



Source: Towey, Giulia & Fabio, Rosa & Capri, Tindara. (2019). Measurement of Attention.

Benton Form Discrimination Test



Source: Towey, Giulia & Fabio, Rosa & Capri, Tindara. (2019). Measurement of Attention.

Pertinent Entrance Examination Findings

- DVAsc: 20/100 OD/OS – Snellen High Contrast
- NVAsc: 20/400 OD/OS – LEA numbers
 - Attempted with continuous text ; (+)alexia
- EOMs: Grossly full OU ; episodes of refixation
- Pupils: PERRL (-)APD

Foveal crowding in posterior cortical atrophy: a specific early-visual-processing deficit affecting word reading

- Very **early** symptom of posterior cortical atrophy
- Similar to crowding phenomenon seen in **amblyopia**
- Compatible with previous reports that state that **flanking effect** strengthened by **increasing proximity**



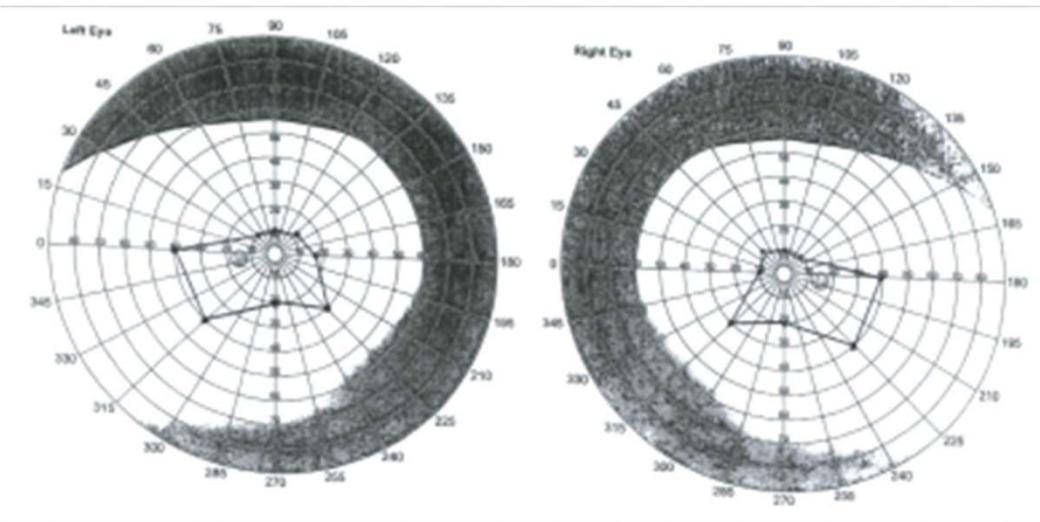
Source: Crutch, S. J., & Warrington, E. K. (2007). Foveal crowding in posterior cortical atrophy: a specific early-visual-processing deficit affecting word reading. *Cognitive Neuropsychology*, 24(8), 843–866. <https://doi.org/10.1080/02643290701754240>

Refractive Assessment

- DVAsc: 20/40 OD/OS – Snellen High Contrast **Single Letter**
- NVAsc: 20/100 OD/OS – LEA numbers **Isolated**
- No change in VAs following refraction

Additional Pertinent Findings

- Farnsworth Large D-15: Unclassified OU
- Contrast Sensitivity:
 - Unable to acquire
 - Presumed moderate or severe
- Arc Perimetry Visual Fields
 - See next slide



IS THERE ANYTHING WE CAN DO?

GOAL 1: READING



GOAL 2: DISTINGUISH FOOD ON PLATE



GOAL 3: INCREASE MOBILITY



Case 4 Clinical Pearls

- Refer to **rehabilitative optometrists** for
 - Visuoperceptual testing
 - Assessment of neurodegenerative patients who **you perceive as complex**
- **Crowding phenomenon** can presents in neurodegenerative patients
 - Posterior Cortical Atrophy → early stages
 - Remaining neurodegenerative conditions → later stages
- CCTVs with ***print to speech*** capabilities are viable options for cognitively unimpaired individuals
- **SUNU bands** paired with **white canes** can increase patient
 - Safety
 - Independence

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