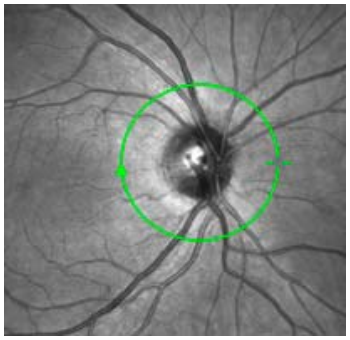
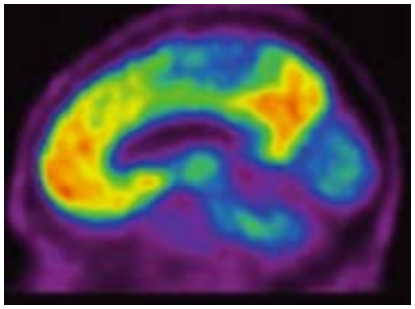
Visual Dysfunction in Alzheimer's Disease and Parkinson's Disease





Victoria S. Pelak, MD
Professor of Neurology and Ophthalmology
Divisions of Neuro-ophthalmology and Behavioral Neurology
University of Colorado School of Medicine

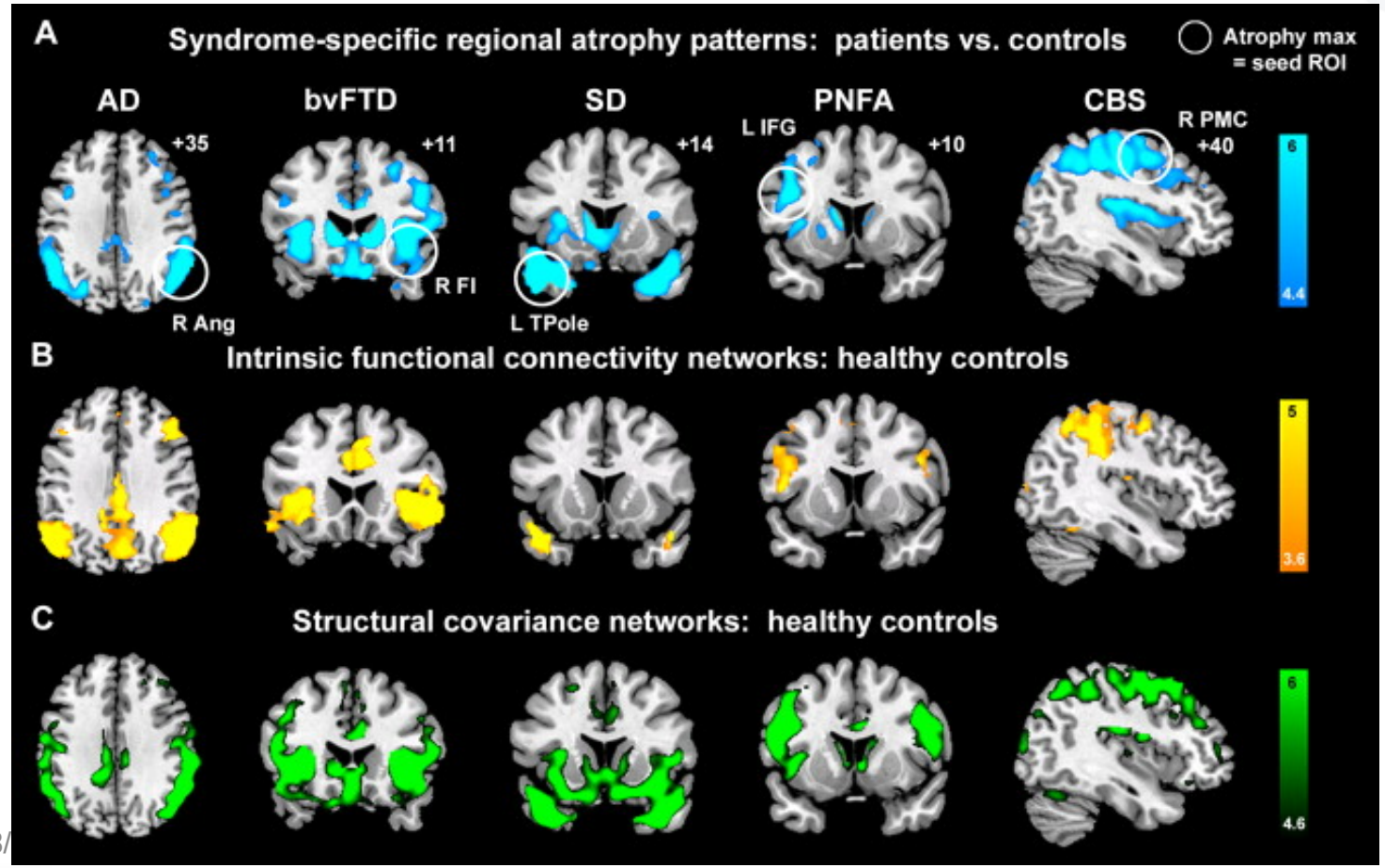
Outline

1. Update: new understanding of visual dysfunction in Alzheimer's Disease (AD) and what you can do in the clinic to recognize it.

2. Review symptoms of visual dysfunction in Parkinson's Disease (PD) and treatment options.

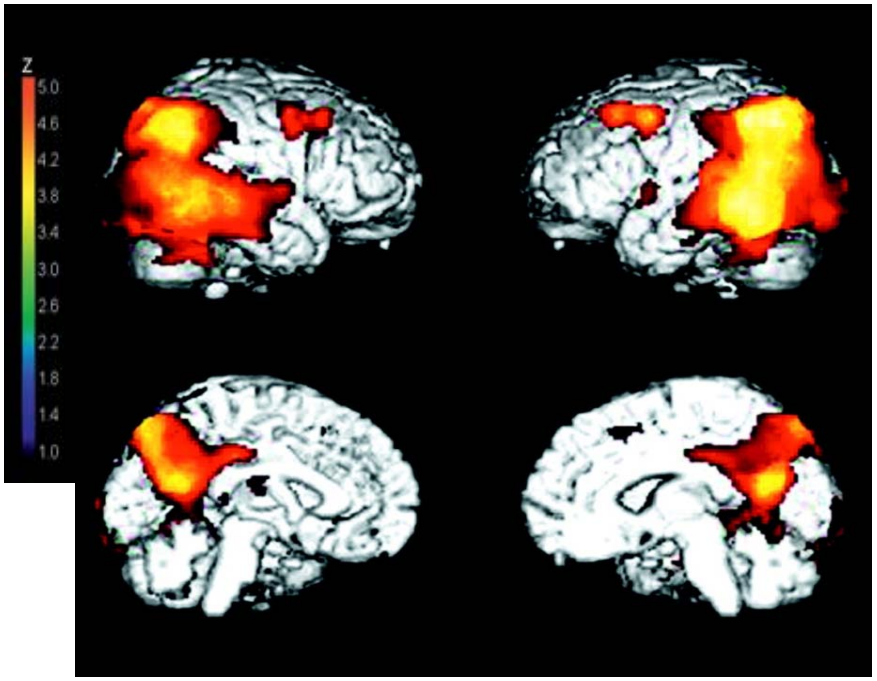
3. Review retinal optical coherence tomography (OCT) as visual biomarker for AD and PD.

Neurodegenerative Diseases Target Specific Brain Networks Disrupt Functional and Structural Connectivity

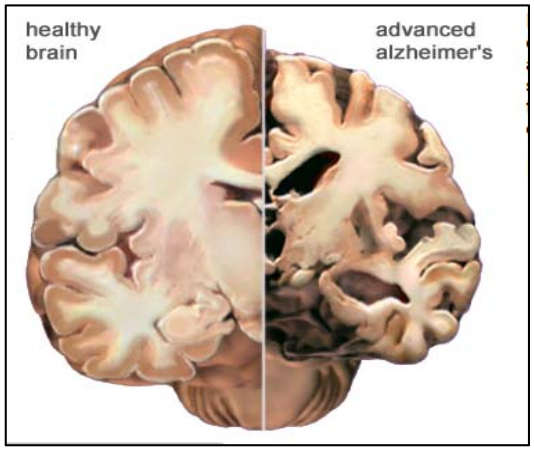


Seeley et al. Neuron 2009

Alzheimer's Disease (AD): Early Hypometabolism in Temporoparietal



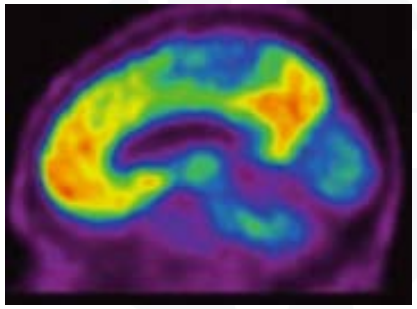
Am J Psych 2002 FDG PET



Alz Association

Why does visuospatial dysfunction occur in later stages of disease?

Alzheimer's Disease (AD)



Typical and atypical presentations of AD can have *prominent visual dysfunction* in the earliest stages of disease due to posterior cortical *network dysfunction*

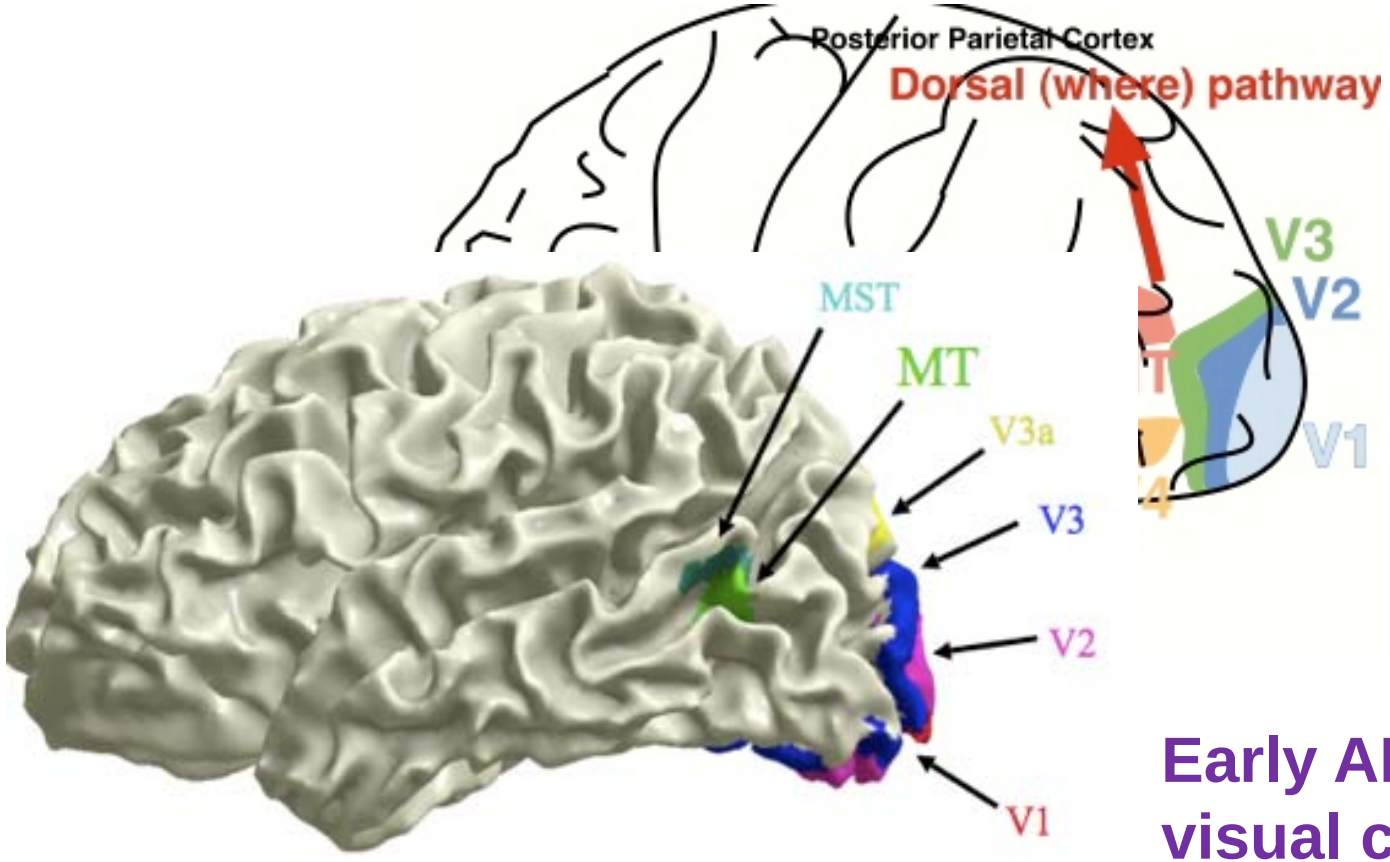
More sensitive tests

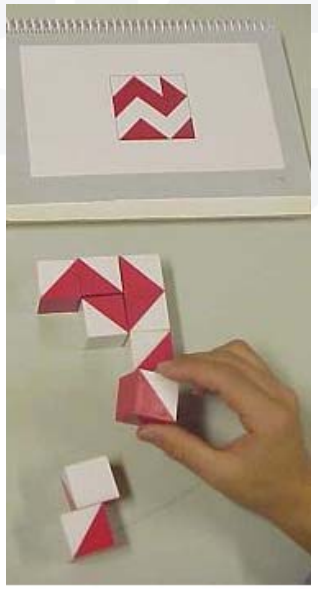
Alzheimer's Disease (AD)

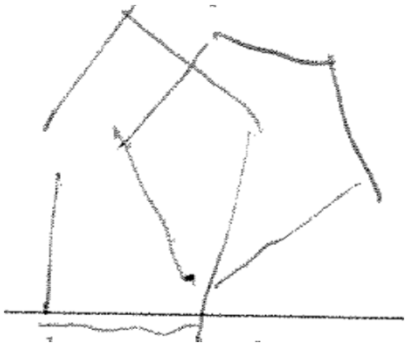
- Typical AD:
  - 1/3 present with vis dysfunction

- Atypical AD patterns:
  - Visual (posterior cortical atrophy)>>>
  - Executive (frontal variant)
  - Language (primary progressive aphasia)

Lack of sensitive tests:
AD Visual Cortical Dysfunction

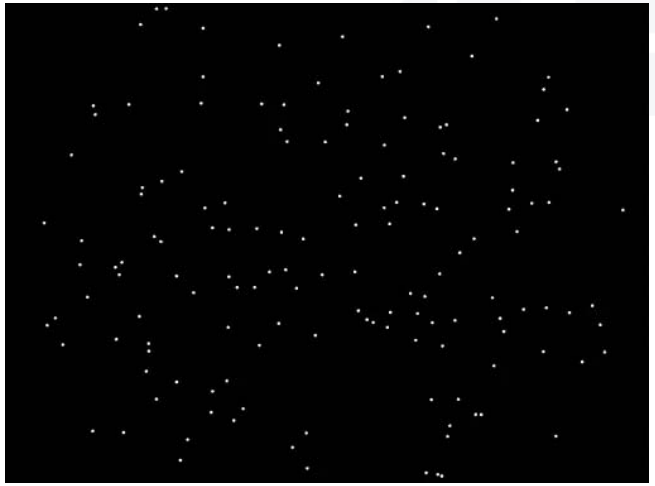






Early AD
visual complaints

Future



Task Development to Increase Sensitivity:

3D virtual reality-based tasks

motion perception & dynamic object recognition

Goals: understanding *disease mechanisms* and aiding in the *early diagnosis of AD*

Now: Enhance Recognition Visual Dysfunction in AD?

Multitude of higher order visual processing deficits

- Visuospatial
- Motion detection
- Visual attention
- Ocular motility patterns

Complaints: Can't see well while reading, driving, using the computer, looking at spreadsheets, etc…

Assessing Visual Complaints

- List*
- Eliminate ocular disease
- And
- Referral formal neuro-cognitive testing
- Non-conventional visual testing*

A brief summary of the concerns discussed follows:

List

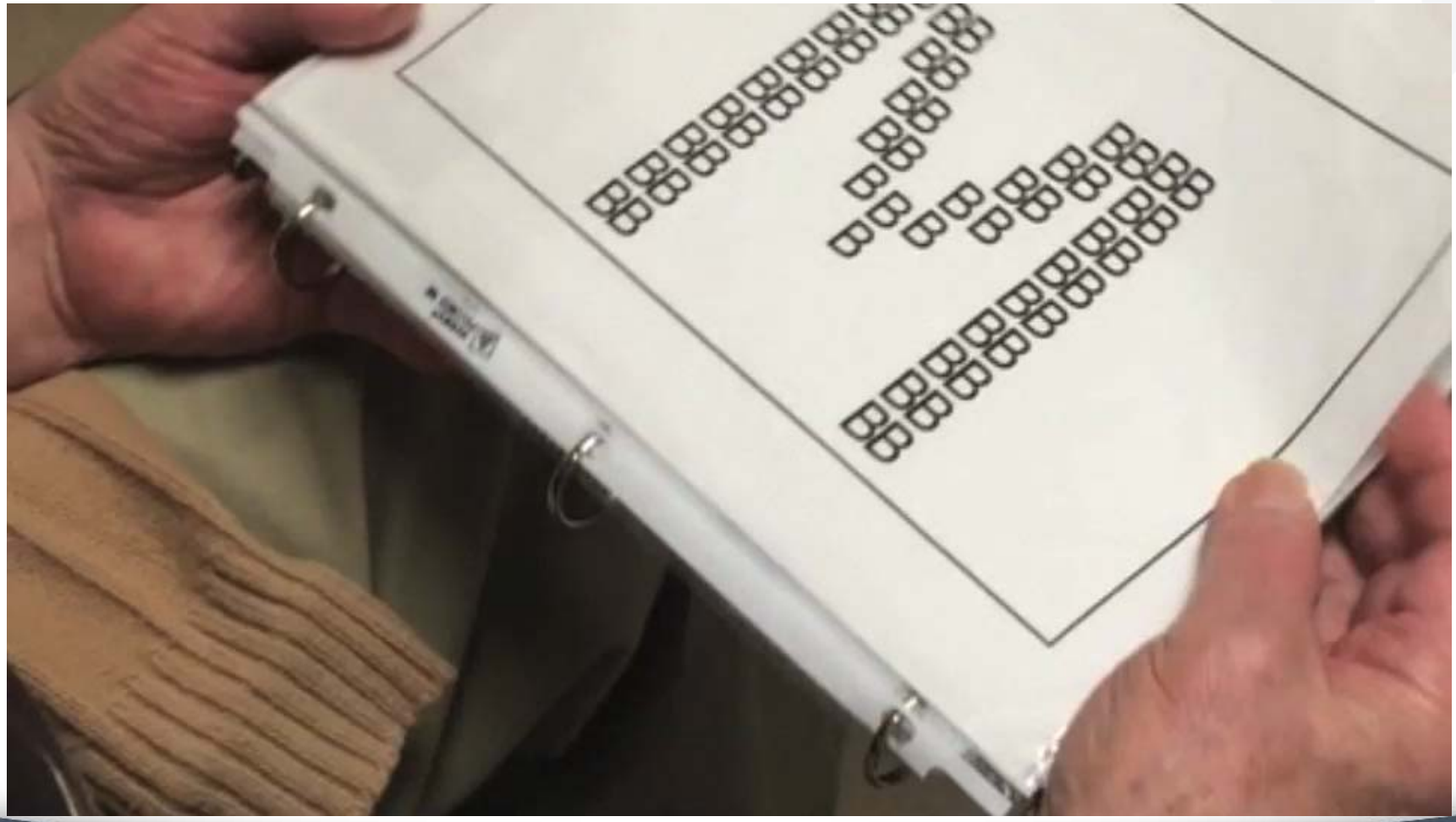
VISION

1. Reading- Basically, can no longer read newspapers, books, or magazines and many important documents Can not read cursive writing at all
2. Writing - Very difficult to print legibly, cannot write cursive - except his name
3. Depth Perception- Has virtually none-frequently can't see stairs, curbs, bumps or holes
4. Color – Misidentifies colors, no differentiation between shades of same color, unable to see objects on surface of similar color
5. "Braille System" - Uses fingers to feel around in order to find objects, such as door knobs, dining utensils, light switches etc.
6. Spatial Relationships – Misses items being handed to him
7. Double Vision – Experienced at times - especially when tired - it helps if he blinks
8. Misidentifying objects – Examples: close up: sees a ketchup bottle for lemonade glass or a candle for a salt shaker distance: golf cart for tow truck or a car for construction vehicle

FUCTIONAL ACTIVITIES

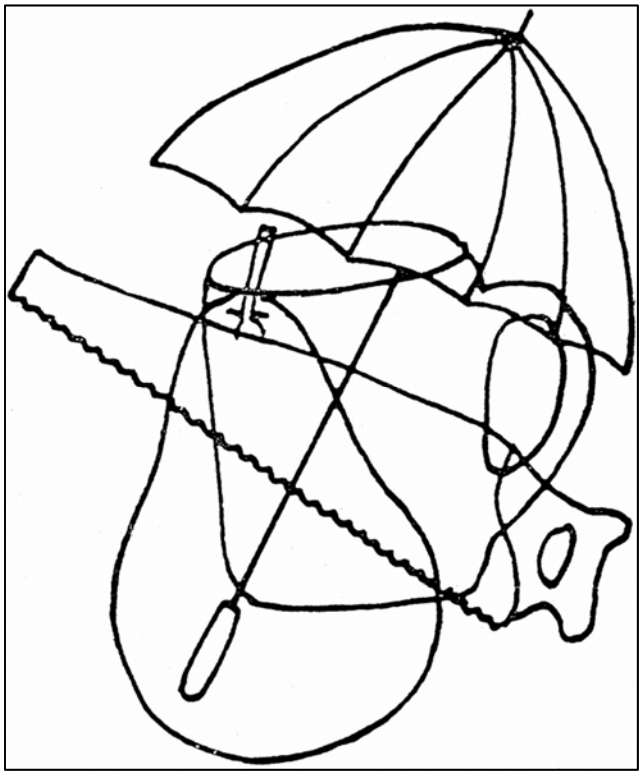
9. Difficulty using – remote controls, phone key pads, computer etc.
10. Misplaces objects – has difficulty finding things - examples: glasses, wallet etc.
11. TV viewing is compromised
12. Does not want to put things away because of the fear of losing them
13. No longer drives due to his own concerns and those of his friends and family
14. Lacks previous excellent sense of direction
15. Vision problems are sometimes compounded by short term memory issues

Non-conventional Vision Testing
Navon letter test

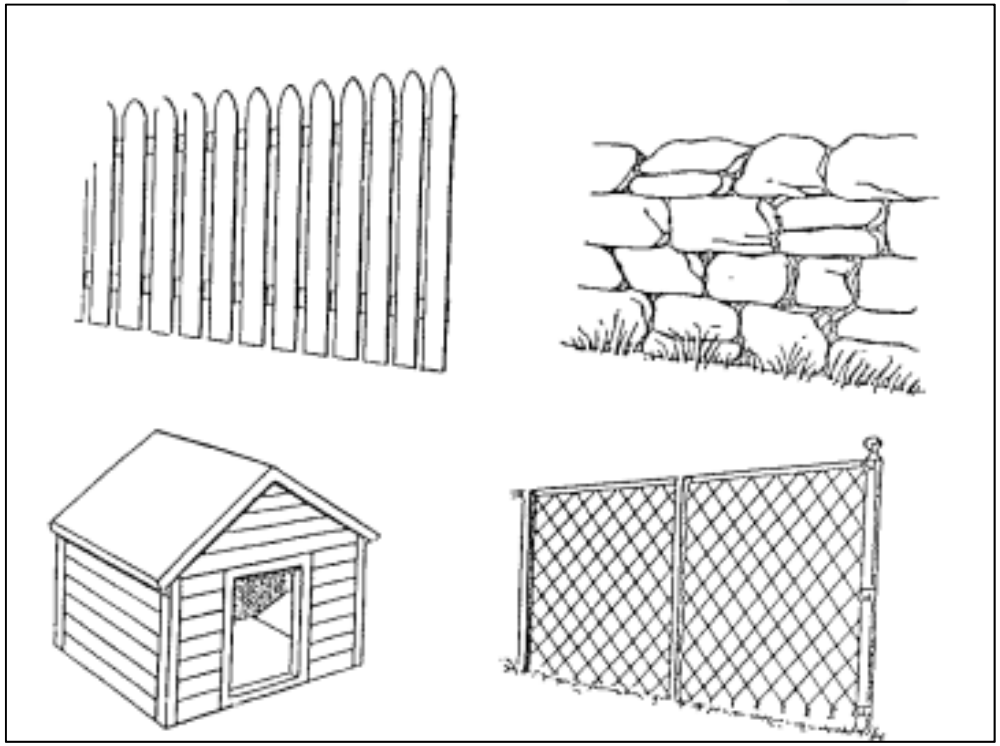


Non-conventional Vision Tests

Ghent's overlapping figure test



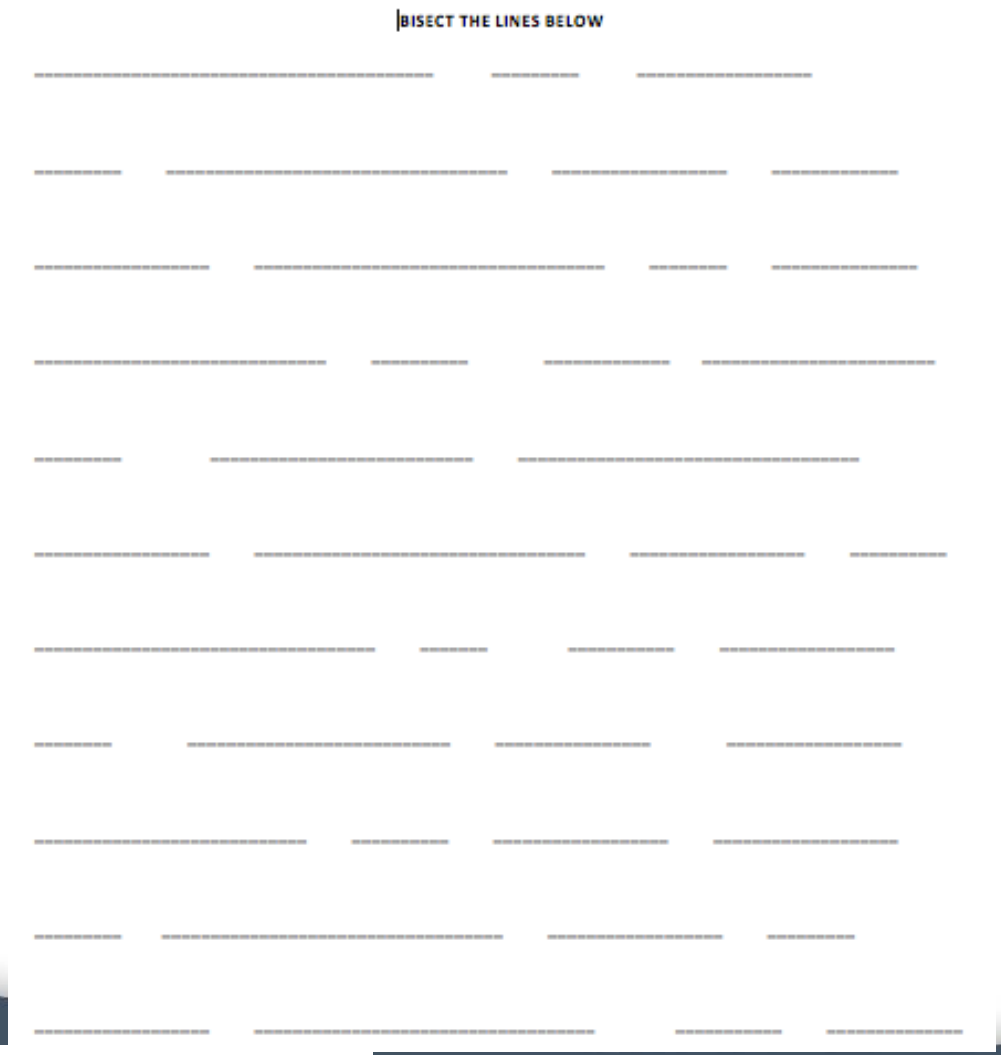
Columbia Mental Maturity Test – Odd Object

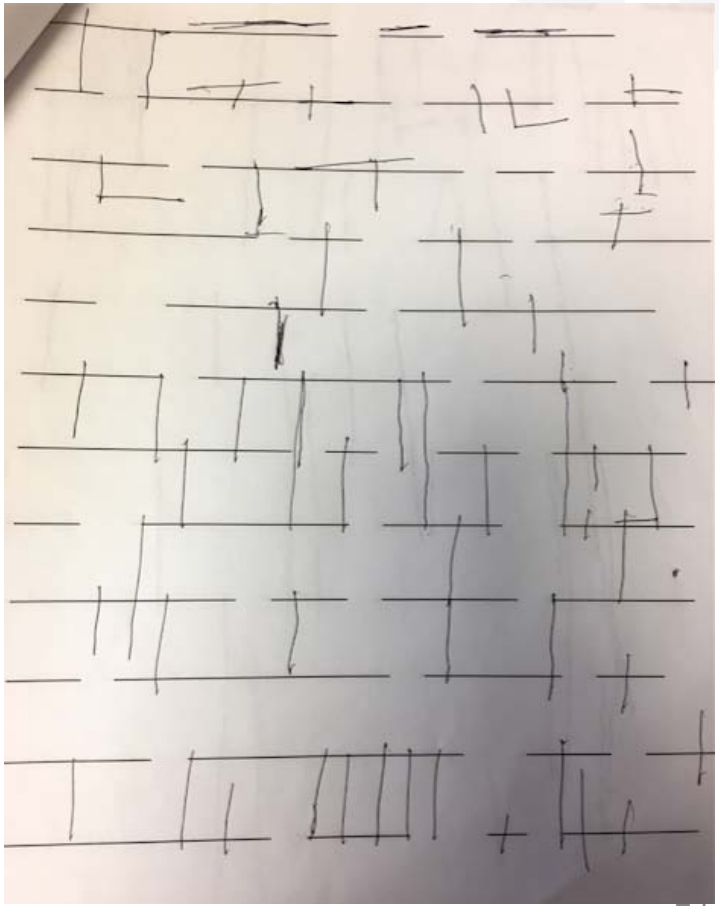


P. Giannakopoulos et al. Neurology 1999;52:71

©1999 by Lippincott Williams & Wilkins

Non-conventional Vision Tests





Can we treat?

- Optimize ocular health
- Identify the function that is impacted
  - Driving, reading, computer use
- Occupational Therapy
- Supportive technology
  - e.g. mobile applications for low sighted

Visual Dysfunction and Parkinson's Disease

1. Basic vision impairment
   - Decreased contrast and color vision
2. Eyelid / blink frequency impairment
   - Decreased blink rate leads to severe dry eye
3. Eye movements abnormalities
   - Convergence insufficiency
4. Perceptual dysfunction (cortical Lewy Bodies)
   - Decreased depth perception, visual illusions, all the same issues seen in AD

1. Basic Vision: Contrast and Color

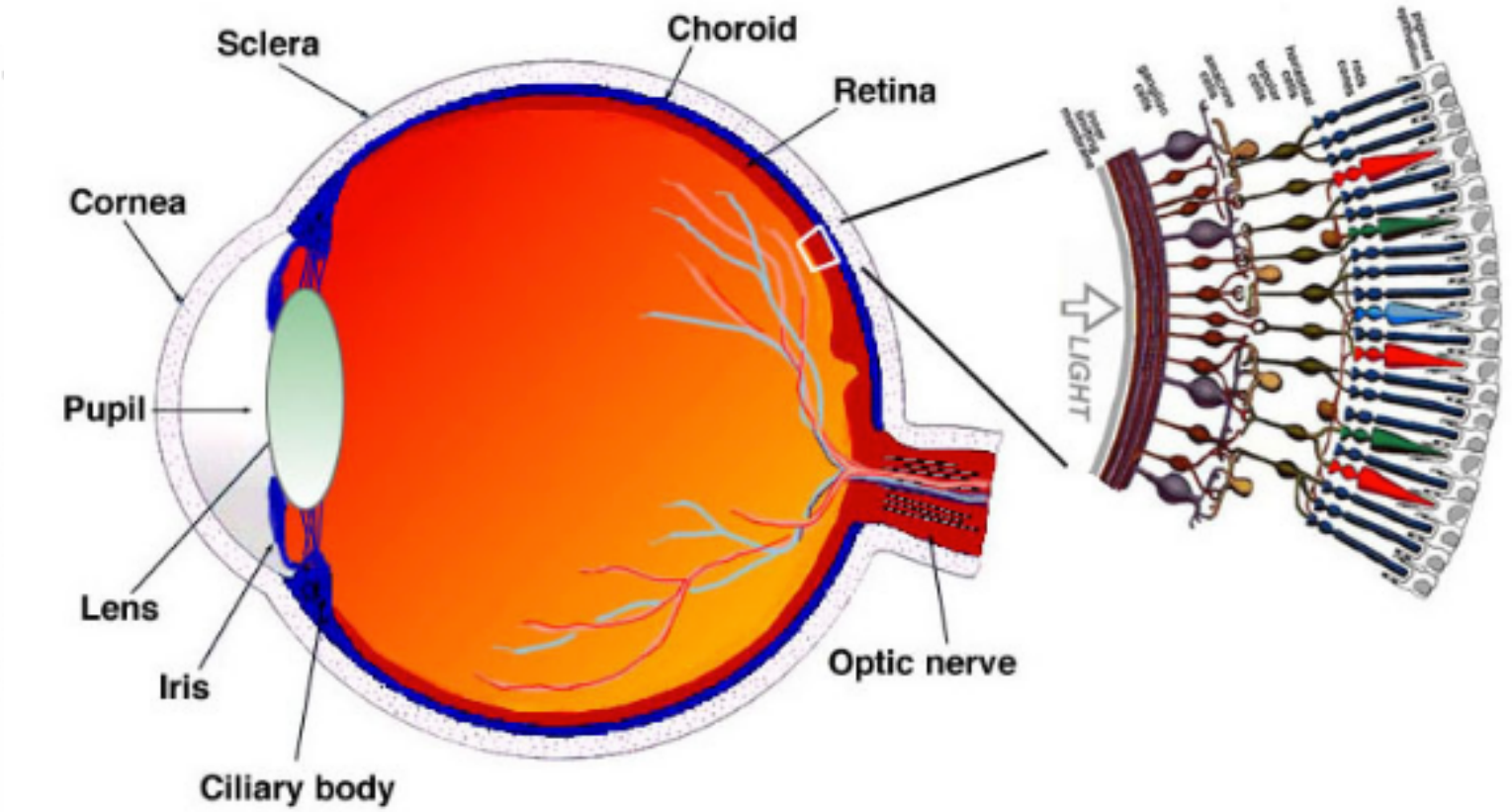


Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.

2. Eyelid: Decreased blink rate

- Leads to dry eye

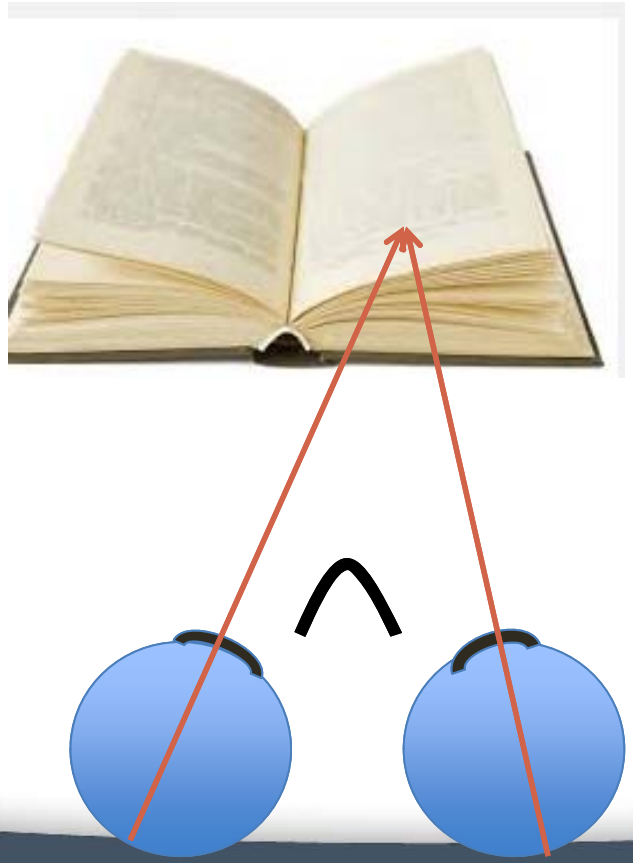
- What is normal blink rate?

A. 25 times a minute
B. 15 times a minute
C. 5 times a minute

- Conversation
- Rest
- Reading

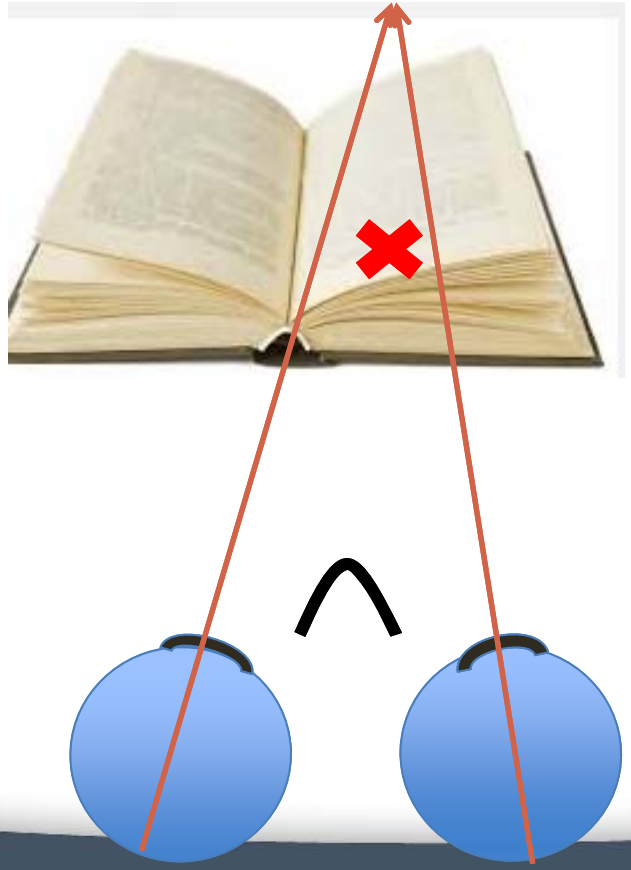
3. Eye movements: Convergence insufficiency

- double vision, blurred vision while reading



3. Eye movements: Convergence insufficiency

- double vision, blurred vision while reading



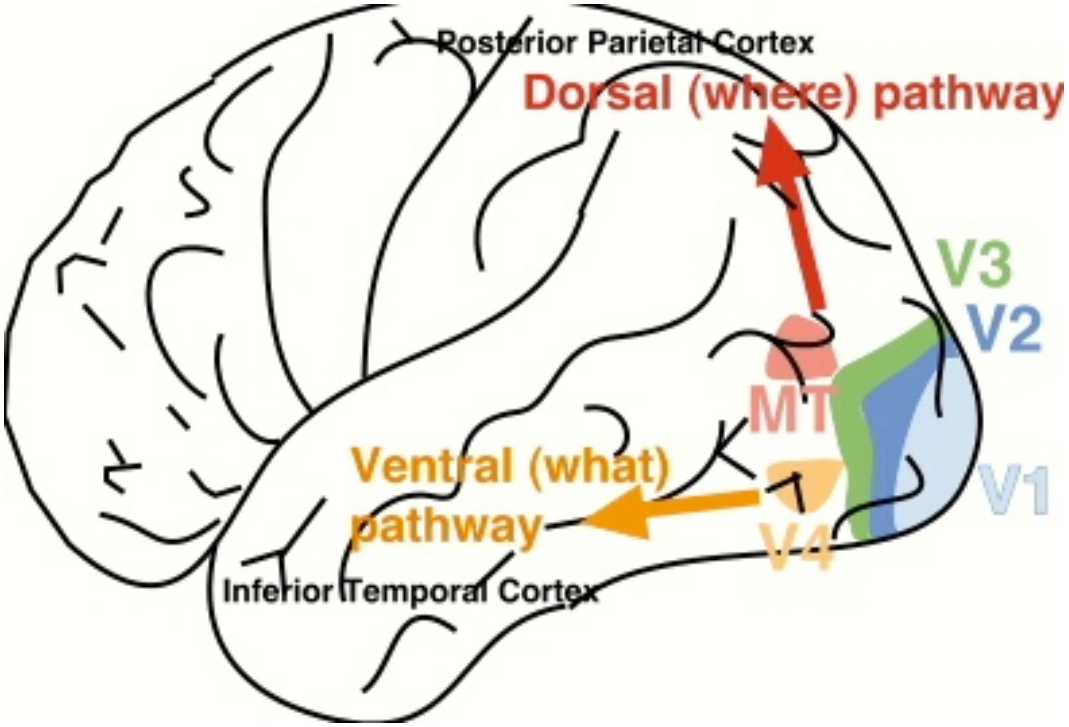
3. Eye movements: Convergence insufficiency

- Treat:
  - prism lenses
  - optimize dopaminergic medications
  - rarely useful to do eye “exercises”

OTHER:

- Separate reading glasses and distance glasses
- Progressive, trifocals, bifocals can make it worse

4. Visual Perceptual



PD

Parkinson's and Visual Quality of Life

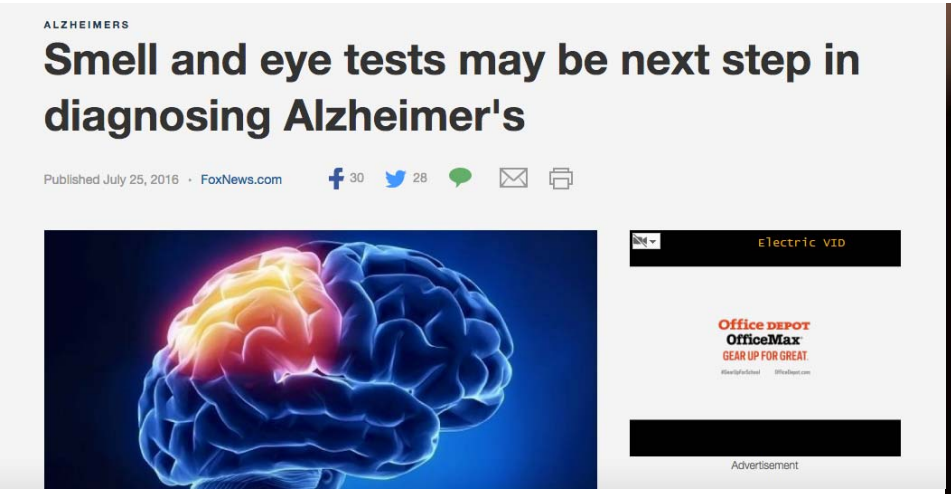
Kirwan Study 2012

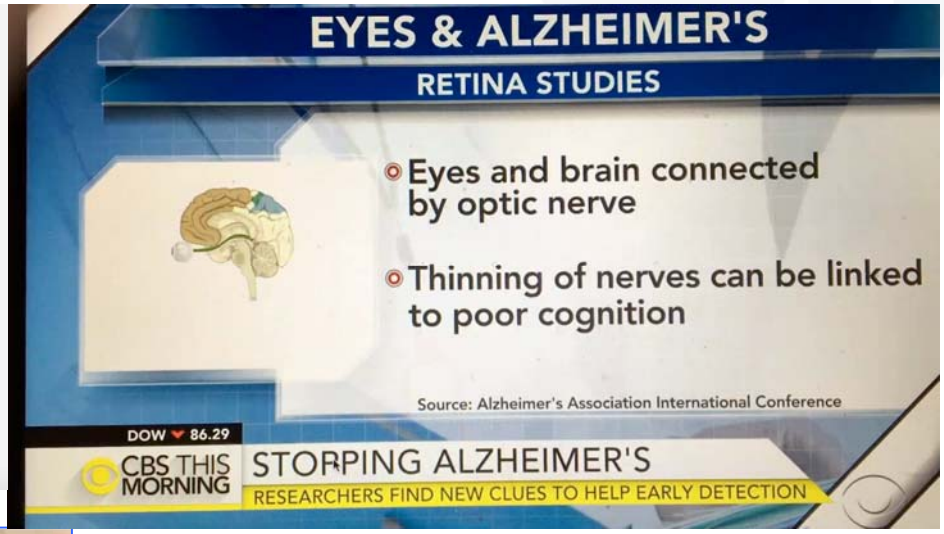
10 point difference (87 v. 97)

Subscales of the National Eye Institute 25-Item Visual Function Questionnaire

Subscale	No. of Items
General health	1
General vision	1
Ocular pain	2
Near activities	3
Distance activities	3
Vision specific	
Social functioning	2
Mental health	4
Role difficulties	2
Dependency	3
Driving	2
Color vision	1
Peripheral vision	1

AD and PD Biomarkers:
Retinal Optical Coherence Tomography

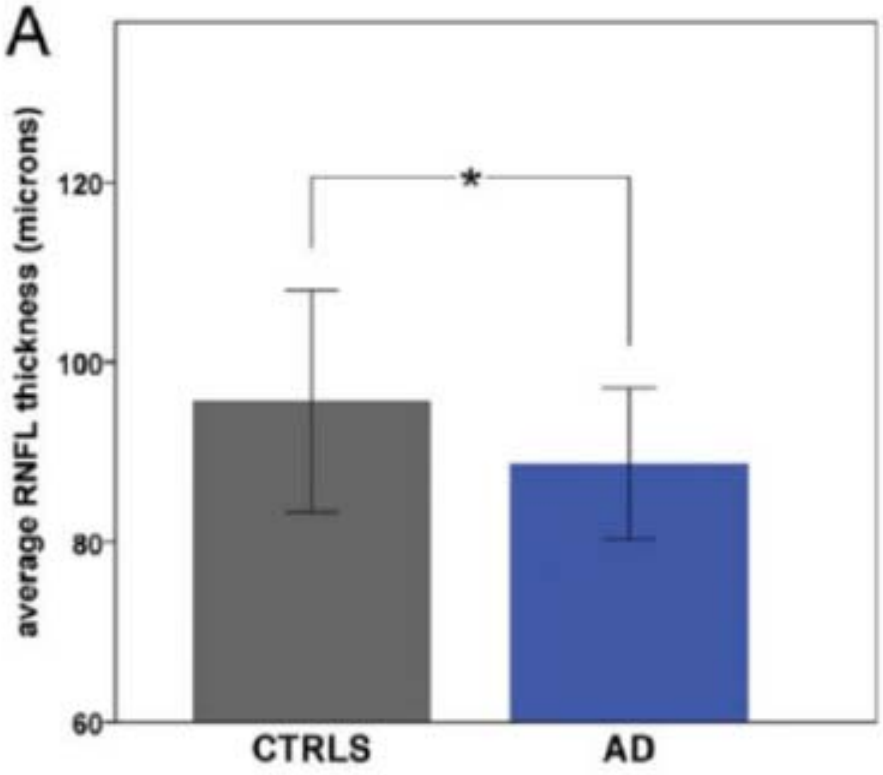


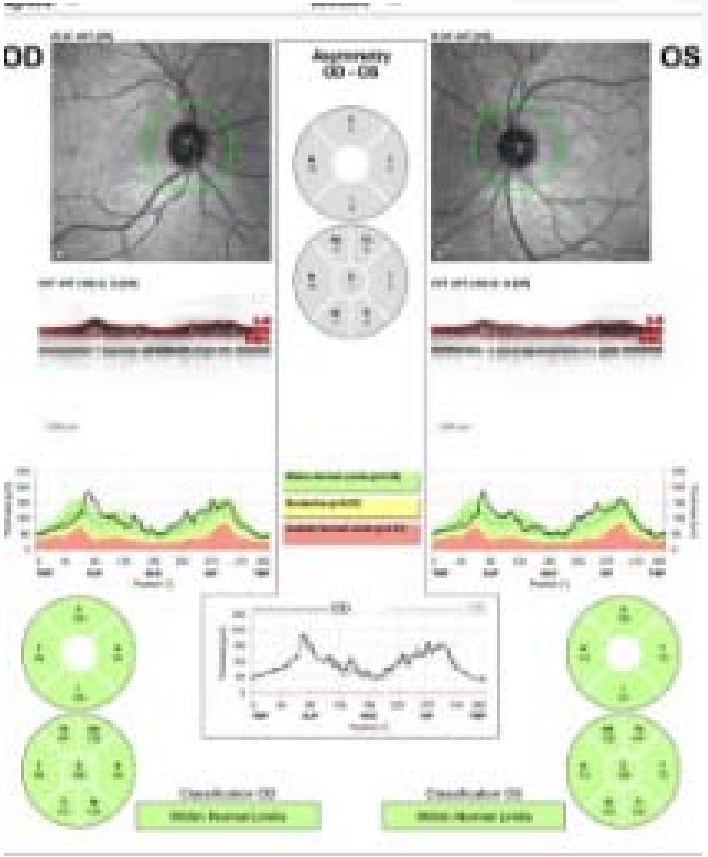


Structure and disease	Finding in Humans
Retina **AD* and PD^**	loss and degeneration inner retinal layer RETINAL GANGLION CELL and AXONS Measure: OCT studies and post-mortem histopathology
Optic nerve **AD**	Axon loss and degeneration post-mortem Intracranial portion with angiopathy post-mortem

*Coppola et al. *PLOS One* 2015
^Yu et al. *PLOS One* 2014

Useful in clinic?

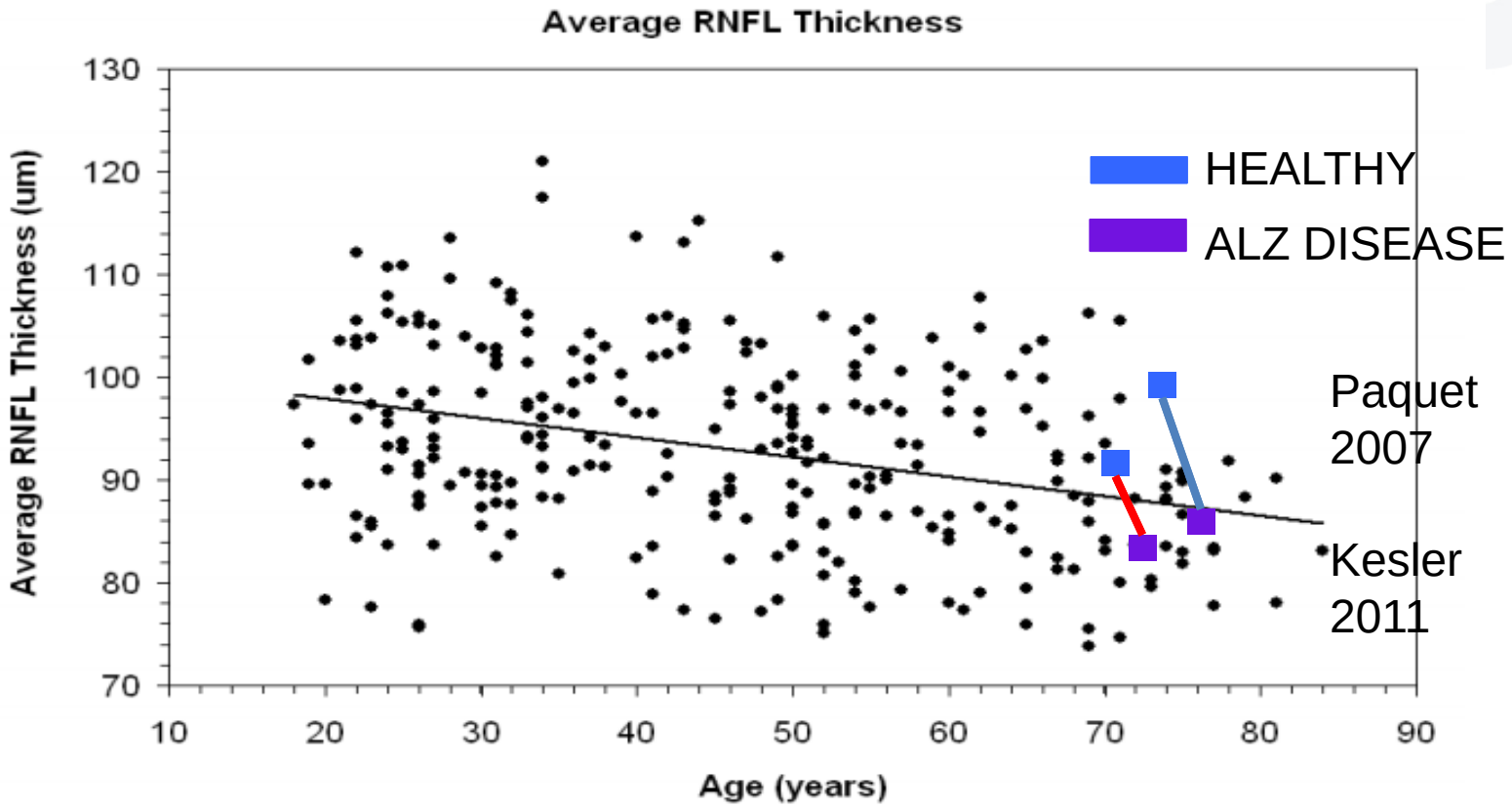




La Morgia 2015

OCT in AD Published studies

Cirrus HD Normative Database

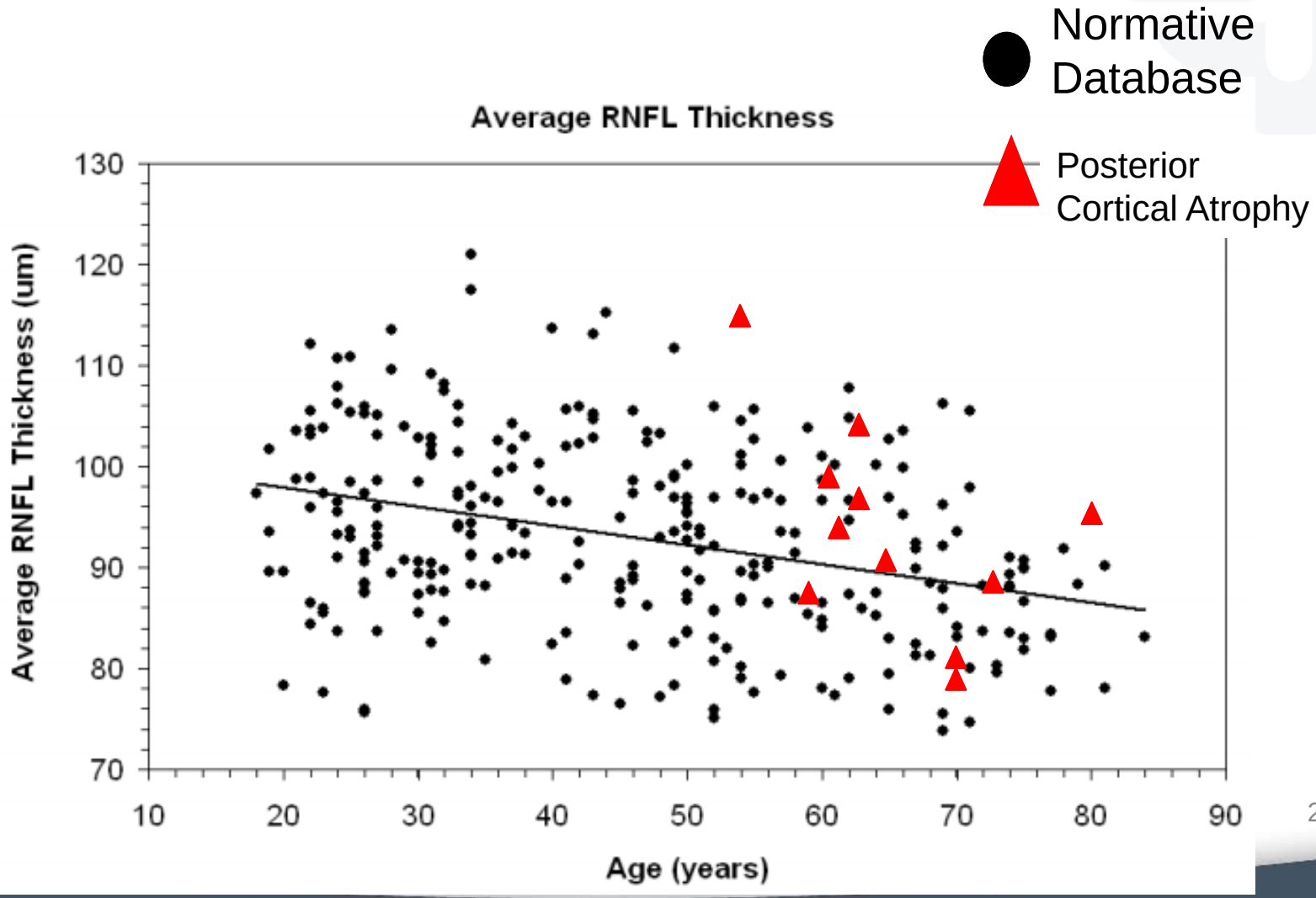


University of Colorado Anschutz Medical Campus

UCHealth

University of Colorado AD: Posterior Cortical Atrophy

Cirrus HD Normative Database



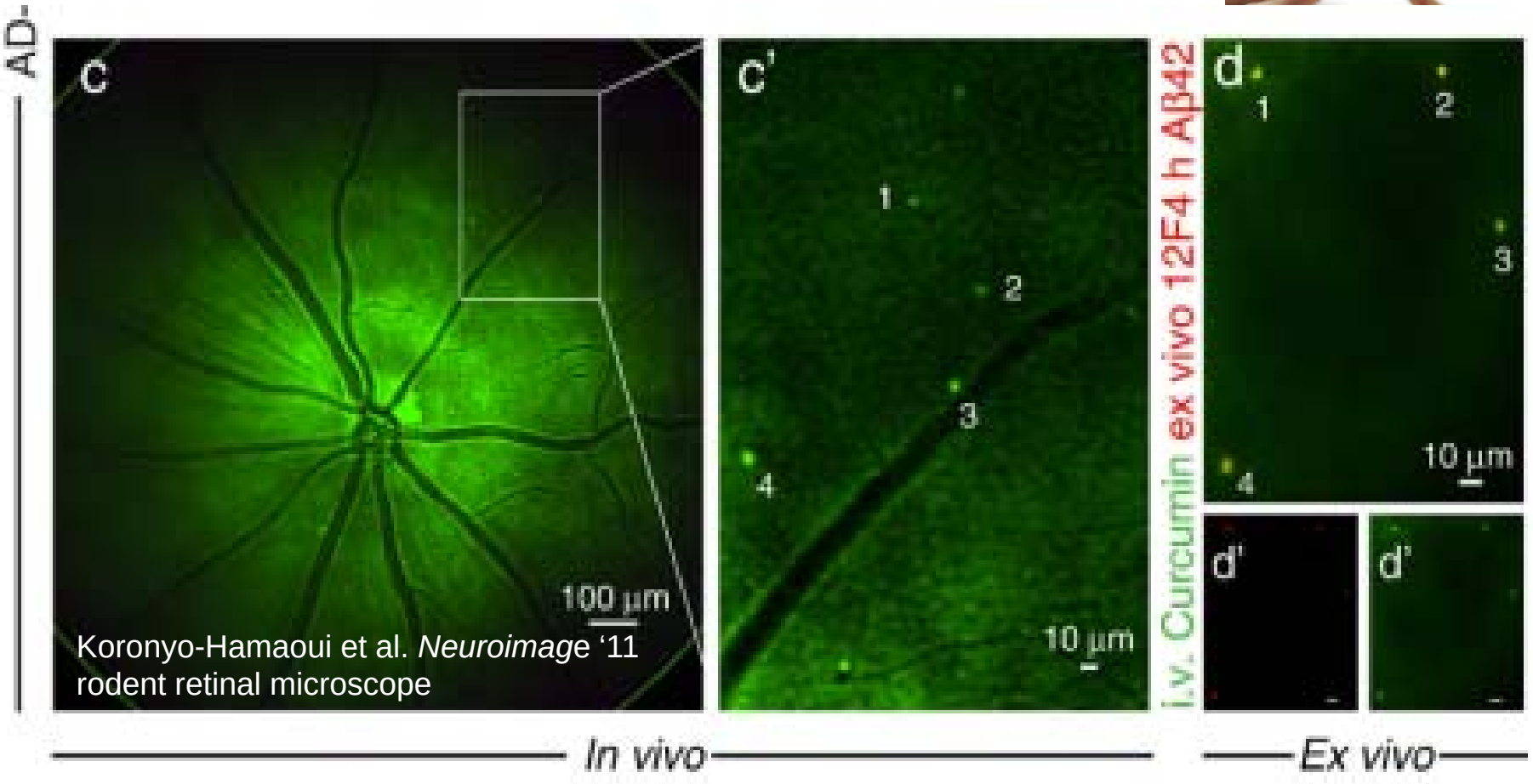
Mice models of Alzheimer's Disease (AD)

More et al. IOVS June 2016
Hyperspectral endoscopic amyloid imaging

spectral imaging

amyloid deposits
specific spectral

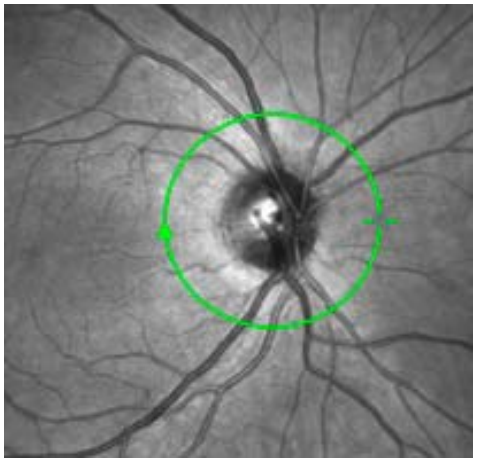
Mice models of Alzheimer's Disease

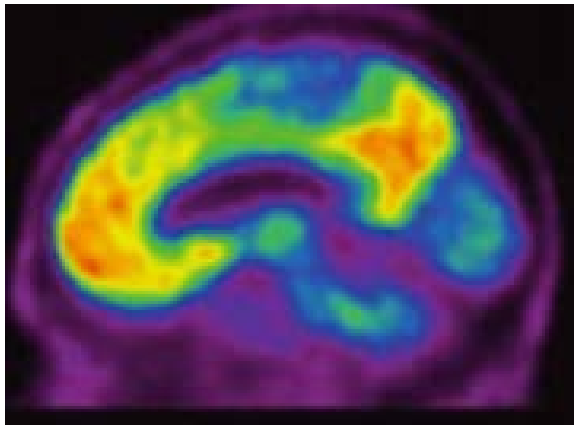


Koronyo-Hamaoui et al. *Neuroimage* '11
rodent retinal microscope

Stay tuned

Thank you



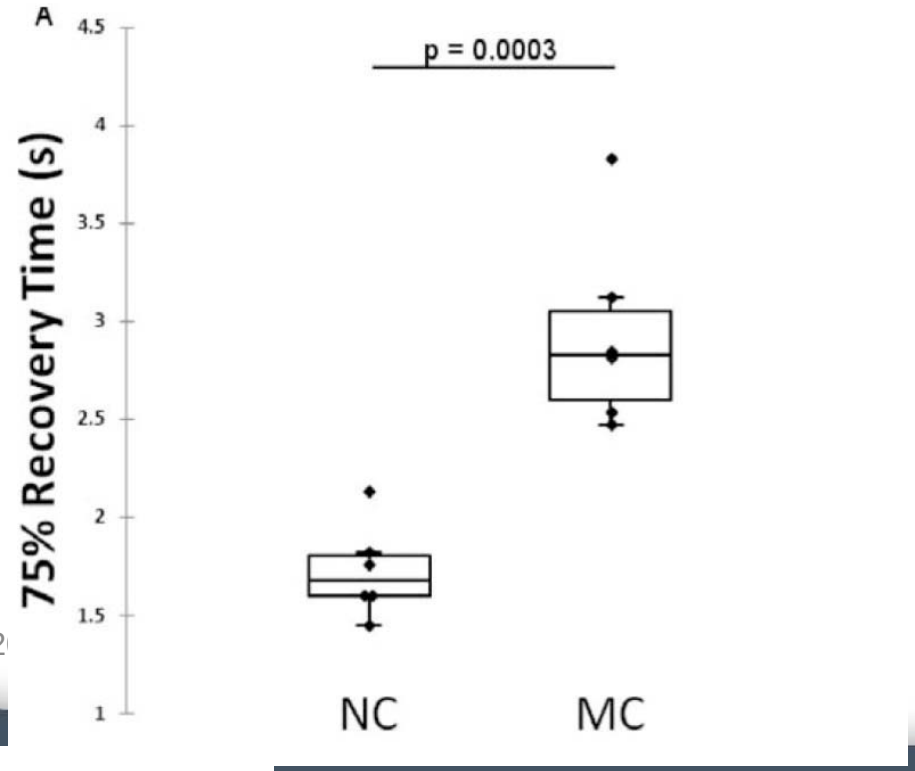


AD: Pupillary Light Reaction

790 *Current Alzheimer Research*, 2013, *10*, 790-796

Pupil Response Biomarkers Distinguish Amyloid Precursor Protein Mutation Carriers from Non-Carriers

Shaun M. Frost[1,2,3], Yogesan Kanagasingam[1,2], Hamid R. Sohrabi[3,4], Kevin Taddei[4], Randall Bateman[5], John Morris[5], Tammie Benzinger[5], Alison Goate[5], Colin L. Masters[6] and Ralph N. Martins[4,*]



MC:

- APP mutation (CAA) and normal cognition