Alzheimer’s Disease and the Visual System

Sam Crish, PhD
Associate Professor
NEOMED
Our Team

Christine Dengler-Crish, PhD

Gina Wilson

Matthew Smith

Emily Plyler

Josephine Lepp
Alzheimer’s disease (AD)

- Chronic, age-related neurodegenerative disease
- Responsible for most dementia in people over 65
- Memory loss, disorientation, mood swings
- 6th leading cause of death in America
AD Pathophysiology

- Plaques – abnormal aggregation of amyloid-beta (Aβ)
- Tangles – intraneuronal accumulation of hyperphosphorylated tau (pTau)

Treatments

• Only treat symptoms, there is no disease-modifying therapy

• By the time it is diagnosed, extensive damage has occurred
Visual problems in AD

• Visual defects in AD have been known for over 30 years (Cogan, 1985)
• Problems in the brain are often accompanied by problems in the retina
• Recent reports indicate that AD-related changes in the retina may occur **YEARS** before cognitive deficits are seen!
So what does this mean?

1. There is a strong need to address vision loss in AD

2. The eye can be a biomarker for Alzheimer’s disease

3. The retina can provide us with a tool for studying AD

4. We can use what we know about AD to inform research and treatments for vision disorders like AMD and glaucoma.
Biomarker for Alzheimer’s disease I: Optical Coherence Tomography (OCT)
Biomarker for Alzheimer’s disease II: Fundus Imaging

Amyloid plaques labeled with curcumin

Curcumin staining of postmortem human retina

Non-invasive imaging of Aβ plaques


Our research

1. How does AD-related pathology affect the retina and its projection in glaucoma and other visual disorders?

   a. Identify new targets for intervention
   b. Identify potential biomarkers

3. Develop and test new therapies for these neurodegenerative conditions.
The relationship between AD & primary visual disorders

- Elevated incidences of glaucoma, AMD, and cataract in patients with AD

- Similar causes as AD in these diseases?

- Let’s look at glaucoma...
Our data show that DBA/2J glaucoma model mice experience age-related increases in tau pathology throughout their brains, optic nerves, and eyes.
We also found elevated amyloid-beta levels in the retina and visual brain structures of two different glaucoma mouse models. These levels varied with age.

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The effects of Alzheimer’s pathology on the visual system

Intraocular tau injections

Control dye injection 1 week

Fluoro-tau injection 1 week

GFAP

Amyloid injections

Control

GFAP

Aβ

Transgenic models of AD

CTB Coverage in the Superior Colliculus

11 mo C57BL/6J
3 mo 3xTg
10 mo 3xTg

3xTg male FEM Ellis 3xTg male FEMS

Accuracy of age

3xTg male 3xTg male

11 mo 3xTg
3 mo 3xTg
10 mo 3xTg
Investigating new therapeutic options: Fingolimod

• FDA-approved oral therapy for multiple sclerosis

• Works to combat MS by reducing neuroinflammation
  • (I haven’t shown you any of that, but it’s another aspect of neurodegeneration we care a lot about)

• It can also reduce tau pathology!
Fingolimod treatment reduces tau pathology in glaucoma
Evidence that fingolimod may improve eye-brain communication in glaucoma
Conclusions

• Alzheimer’s disease affects the visual system

• Interdisciplinary collaboration is key: knowledge gained from vision research can help inform AD research and vice versa
Thank you!