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

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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

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:

**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.

**FUNCTIONAL 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
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

![Diagram of human eye](www.testingcolorvision.com/test-examples.php)

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
Parkinson’s and Visual Quality of Life

Kirwan Study 2012
10 point difference (87 v. 97)
AD and PD Biomarkers:
Retinal Optical Coherence Tomography
<table>
<thead>
<tr>
<th>Structure and disease</th>
<th>Finding in Humans</th>
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</thead>
<tbody>
<tr>
<td>Retina AD* and PD^</td>
<td>loss and degeneration inner retinal layer RETINAL GANGLION CELL and AXONS Measure: OCT studies and post-mortem histopathology</td>
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<tr>
<td>Optic nerve AD</td>
<td>Axon loss and degeneration post-mortem Intracranial portion with angiopathy post-mortem</td>
</tr>
</tbody>
</table>

*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

Average RNFL Thickness

- HEALTHY
- ALZ DISEASE

Paquet 2007
Kesler 2011

Age (years)

Average RNFL Thickness (um)
University of Colorado AD: Posterior Cortical Atrophy
Cirrus HD Normative Database

Average RNFL Thickness

Age (years)

Average RNFL Thickness (um)

Normative Database

Posterior Cortical Atrophy
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

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

Shaun M. Frost¹,²,³, Yogesan Kanagasingam¹,², Hamid R. Sohrabi³,⁴, Kevin Taddei⁴, Randall Bateman⁵, John Morris⁶, Tammie Benzinger⁵, Alison Goate⁵, Colin L. Masters⁶ and Ralph N. Martins⁴,*

MC:
- APP mutation (CAA) and normal cognition

N=6  N=6