Are Saccadic Eye Movements a potential biological marker for Alzheimer’s disease?

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Dementia: A Global Problem

- 4.6 million new case/yr world wide
- By 2025 71% people with dementia based developing countries: biggest impact India, China.
- Many western psychological tests are NOT suitable for developing countries. Valid diagnostic tests across cultures.
The pathology begins many years before clinical symptoms!

- Some people may already have the very early stages of AD!

- Pathology in AD commences roughly 20–30 years prior to diagnosis.
  (Schneider, Hampel & Buerger 2009)

“...the disease may develop silently for many years before symptoms appear”

Alzheimer’s Society.
Alzheimer’s Disease: The Diagnostic Problem

• Psychological Diagnosis, rests on gradual decline of short term memory.

• By the time this appears, brain damage is too severe to be reversed or halted.

• Currently no medication is able to reverse or slow down damage, probably too late.

• Urgent need for early diagnostic markers
Saccadic eye movements controlled by cortical and subcortical networks
Where you look reflect cognitive processes – ("What are they wearing?" 2010- Gordon & Sarah Brown)
(How many windows in No. 10 Downing Street?)
Phase 1:
Three Research Questions

1. Can tests of saccadic eye movements detect dementia in the early stages of Alzheimer’s disease?

2. Can these tests provide a measure of the severity of dementia as the disease progresses?

3. Are the disease effects distinct from normal aging?
Phase 2: Three Research Questions (EPSRC UK Research Grant).

1. Can tests of saccadic eye movements distinguish between different types of cognitive impairment (aMCI vs naMCI)?

2. Can machine learning help with the diagnosis?

3. Can we diagnose in the home using non-stress everyday tasks: Watching TV making tea?
Phase 3: Research Questions
(Funding needed).

1. Can we cure Alzheimer’s disease using a flashing light?
Participant Groups

- **Mild Alzheimer’s disease - mild (N=19)**
  
  MMSE = 21 / ADAScog = 22.8

- **Older Controls (N=32)**
  
  MMSE = 29 / ADAScog = 7.8

- **Young Controls (N=17)**
3471 Cognitive Assessments
Correct Anti-Saccade

Target (4°)

Visual field (deg)

-400 -200 0 200 400 600

-15 -10 -5 0 5 10 15

a Central fixation
b Primary saccade latency
c Primary saccade amplitude
Corrected Error
Uncorrected Errors
Inhibition (anti) task

Uncorrected Errors

- AD: 25
- Seniors: 5
- Young: 3

Comparison of uncorrected errors across AD, Seniors, and Young groups.
Errors correlate with severity of dementia
Can Eye Movements detect dementia before the onset of conventional cognitive symptoms?
Can Eye Movement detect dementia before conventional cog symptoms?
Eye Movements Data

Neuropsychological Assessment

- Anti Gap Errors (%)
- Primary latency
- Corrected errors V Uncorrected errs
- Corrected errors Primary latency
- Corrected errors Secondary latency

- EADAS cog
- SMMSE
- Nart errors
- Nart predicted FSIQ
- Nart predicted Verbal IQ
- Nart predicted Perf. IQ
- Digit Span Forwards
- Digit Span Reverse
- Spatial Span Forwards
- Spatial Span Reverse

Normal
Phase 2:
Three Research Questions
(EPSRC UK Research Grant).

1. Can tests of saccadic eye movements distinguish between different types of cognitive impairment (aMCI vs naMCI)?

2. Can machine learning help with the diagnosis?

3. Can we diagnose in the home using non-stress everyday tasks: Watching TV making tea?
## Phase 2:

<table>
<thead>
<tr>
<th></th>
<th>AD (n=48)</th>
<th>aMCI (n=42)</th>
<th>naMCI (n=35)</th>
<th>CP (n=96)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>73.9 (7.1)</td>
<td>74.1 (7.6)</td>
<td>67.8 (6.3)</td>
<td>66.9 (8.5)</td>
<td>&lt;.0005</td>
</tr>
<tr>
<td><strong>Sex (% male)</strong></td>
<td>53.7%</td>
<td>38.9%</td>
<td>54.3%</td>
<td>37.7%</td>
<td>ns</td>
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<tr>
<td><strong>MoCA score</strong></td>
<td>19.76 (5.3)</td>
<td>20.7 (5.1)</td>
<td>25.1 (2.3)</td>
<td>28.1 (1.9)</td>
<td>&lt;.0005</td>
</tr>
</tbody>
</table>
Antisaccade uncorrected errors

Prosaccade latencies (ms)

Error Correction

<table>
<thead>
<tr>
<th>Condition</th>
<th>Errors</th>
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</thead>
<tbody>
<tr>
<td>AD</td>
<td>0.20</td>
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<tr>
<td>aMCI</td>
<td>0.22</td>
</tr>
<tr>
<td>naMCI</td>
<td>0.18</td>
</tr>
<tr>
<td>CP</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Prosaccade latencies (ms)

- AD: 210 ms
- aMCI: 190 ms
- naMCI: 170 ms
- CP: 150 ms
Heatmap plots of the raw eyegaze signals—AD & aMCI have *long* ‘comet’ tails—naMCI and controls (CP) have *short* “comet’ tails.
Machine learning classification: aMCI vs naMCI
MoDeM Study: The real world
MoDeM Study

1. Free Viewing

2. Directed Viewing a) What color clothes? b) How many windows?
Gordon Brown video resignation:
Phase 3: Research Questions
(Funding needed).

1. Can we cure Alzheimer’s disease using a flashing light?
Can flashing lights cure Alzheimer’s disease?
Conclusions

• Eye gaze discriminates between the effects of normal ageing and disease, and is sensitive to longitudinal effects in AD.

• Eye gaze may provide a promising tool in the early diagnosis of AD.
Thank you!

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