EEG-based Alzheimer’s Disease Diagnosis: Where We are at Now and Where We are Heading

*Tiago H. Falk*

*Institut National de la Recherche Scientifique*

*Energy, Materials and Telecommunications (INRS-EMT)*

*Montreal, Quebec, Canada*
Preamble on Alzheimer’s Disease (AD)
Existing diagnostic tools
Drawbacks and motivation for EEG
Where are we now
Where we are heading
Conclusions
Alzheimer’s Disease: An Epidemic (?)
Worldwide Epidemic

![Graph showing the increase in number of people with dementia (millions) from 2010 to 2050 for low- and middle-income countries and high-income countries. The graph indicates a significant rise over the years, with a steeper increase for low- and middle-income countries.]
Change in Number of Deaths

Change in Number of Deaths Between 2000 and 2010

- Breast Cancer: -2%
- Prostate Cancer: -8%
- Heart Disease: -16%
- Stroke: -23%
- HIV/AIDS: 68%
- Alzheimer's Disease: 42%
Something Needs to be Done

Early Diagnosis Keeps Your Life From Unravelling.

Alzheimer Society
There's So Much To Hold On To.
Neuropsychological examination

- Mini-mental state examination (MMSE)
- Montreal Cognitive Assessment (MoCA)
- 70-90% accuracy
- Lower for MCI (mild cognitive impairment)
- Not very useful for prognosis/progression
Definite Diagnosis

- Definite diagnosis requires post-mortem histopathological analysis of the brain
What is Known

• Beta amyloid plaques
  – “Sticky” protein fragments that are normally broken down and eliminated
  – AD: block cell signaling and blood flow

• Neurofibrillar tangles
  – Microtubule transports nutrients through nerve cell → tau protein abnormal with AD
How is Technology Helping?

- **S-MRI**: detect tissue loss
- **PET**: tracer binds to beta amyloid
- **SPECT perfusion**: assess regional blood flow
Drawbacks & Motivation for EEG

• Tissue loss and atrophies represent late stage of neural dysfunction \( \rightarrow \) early detection (?!?)

• Expensive equipment, experienced personnel
  – Low-income countries, rural and remote areas (?!?)
  – Urban areas: long waiting times (e.g., in Canada: up to 6 months for non-emergency MRI)

• EEG: better suited to reveal functional impairment as it reflects the electrical activity of neural tissue, evident long before actual tissue loss occurs.
Classical EEG Findings (c. 1980’s)

**Resting-Awake**
- “Slowing” of the EEG: increase in EEG delta/theta power and a decrease in alpha/beta
- Inter-hemispheric disconnect (alpha/beta)
- Non-linear dynamics: decrease in complexity

**ERP’s**

<table>
<thead>
<tr>
<th>Lat P300 Fz</th>
<th>Amp P300 Fz</th>
<th>Lat P300 Pz</th>
<th>Amp P300 Pz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>431.78 (21.3)</td>
<td>5.69 (1.85)</td>
<td>445.13 (27.3)</td>
</tr>
<tr>
<td>MCI</td>
<td>537.48 (60.7)</td>
<td>3.50 (1.42)</td>
<td>528.94 (73.4)</td>
</tr>
<tr>
<td>AD</td>
<td>564.31 (6.1)</td>
<td>3.13 (1.59)</td>
<td>568.37 (77.4)</td>
</tr>
</tbody>
</table>
New EEG Features

Hemodynamics involved in information processing via neural activity modulation

![Diagram of EEG bands and computations](image)
Healthy vs. Alzheimer’s

m-delta
m-theta
m-alpha
m-beta
## Experimental Results (22:AD, 12:C)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Accuracy (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coherence (I)</td>
<td>70.6</td>
<td>86.4</td>
<td>41.7</td>
</tr>
<tr>
<td>Power (II)</td>
<td>85.3</td>
<td>90.9</td>
<td>75.0</td>
</tr>
<tr>
<td>PME (III)</td>
<td>88.4</td>
<td>90.9</td>
<td>83.3</td>
</tr>
<tr>
<td>I + III</td>
<td>79.4</td>
<td>86.4</td>
<td>66.7</td>
</tr>
<tr>
<td>II + III</td>
<td><strong>94.1</strong></td>
<td><strong>96.5</strong></td>
<td><strong>91.7</strong></td>
</tr>
<tr>
<td>I + II + III</td>
<td>91.2</td>
<td>96.5</td>
<td>83.3</td>
</tr>
</tbody>
</table>
(Not) Automated and (Not) Portable

• Multi-channel medical (research) grade EEG
  – 20, 32, 64 channels
  – Not portable

• Require visual inspection of artifact-free epochs
  – Remove movement, muscle, eye-blink artifacts
  – Labor-intensive, requires experienced personnel
  – Not automated
Automated and Portable

- Seven-channel portable system
- Automated Artifact Removal (AAR)

- Relevance vector machine (RVM) vs SVM
Experimental Results

• 35 AD, 24 C
• Benchmark: visual inspection + SVM

<table>
<thead>
<tr>
<th>System</th>
<th>Accuracy (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benchmark</td>
<td>84.7</td>
<td>75.0</td>
<td>91.4</td>
</tr>
<tr>
<td>SVM</td>
<td>81.4</td>
<td>75.0</td>
<td>85.7</td>
</tr>
<tr>
<td>RVM</td>
<td>84.7</td>
<td>79.2</td>
<td>88.6</td>
</tr>
</tbody>
</table>

• Advantages over visual inspection:
  – Improved sensitivity relative to benchmark
  – Information from **frontal** electrodes kept
WHAT NEXT?

DON'T TELL ME.
Resting-Awake vs Mental Activity

Alzheimer’s disease

Healthy brain

Cerebral cortex:
Responsible for language and information processing

Alzheimer’s disease brain

The cortex shrivels up, damaging areas involved in thinking, planning and remembering

Ventricles filled with cerebrospinal fluid grow larger

Hippocampus:
Critical to the formation of new memories

Hippocampus shrinks severely

Source: Alzheimer’s Association
Hippocampal Activation

- Working memory
- ERD/ERS

Figure 4. Average topographical maps of the ERD % for NS, MCI and AD groups (from top to bottom) on alpha band and 175-325ms time interval, during execution of the 2-back task (match trials).
Multimodal Neuroimaging

- EEG + fNIRS (near-infrared spectroscopy)
- Areas coincide with alpha modulation features
  – Neurovascular coupling
Conclusions

• Alzheimer’s disease quickly becoming an epidemic
• New biomarkers are being developed, neuro-imaging is playing an important role
  – EEG stands out for its potential, lower cost, portability
• Amplitude modulation insights → new features for diagnosis and disease progression monitoring
• Multimodal solutions → new biomarkers
Acknowledgements

• Collaborators
  – Francisco Fraga, UFABC, Brazil
  – Renato Anghinah, USP, Brazil
  – Natalie Phillips, Concordia, Canada
  – Veronique Bohbot, McGill, Canada

• Students
  – Raymundo Cassani, INRS, Canada
  – Lucas Trambaiolli, UFABC, Brazil

• Funding: INRS (start-up program)
"If the brain were so simple we could understand it,
we would be so simple we couldn’t"

- Lyall Watson