EEG Diagnostics for Mild Cognitive Impairment and Early Alzheimer’s Disease

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Mild cognitive impairment (MCI) and Alzheimer’s disease (AD) are related neurological disorders

- **MCI**
  - Cognitive decline greater than expected for age/history

- **AD**
  - Memory loss
  - Shrinking vocabulary
  - Loss of motor control

- **MCI → AD**
  - 10-15%/year

**Current diagnosis techniques**

- **MCI**
  - Self/family-reported behavior

- **AD**
  - Cerebrospinal fluid (CSF) biomarkers
  - Requires lumbar puncture
EEG screening for MCI/AD would provide benefits for practitioners and patients.

**Binary classification**

- Normal controls (NC)
- MCI
- AD

**EEG**
- Inexpensive
- Less invasive

**Assist with dementia treatment**
- Screening/diagnosis
- Evaluation
- Monitoring
Data included 46 subjects and 3 protocols

- 46 subjects
  - 15 NC
  - 16 MCI
  - 15 AD
- 20 channels
- 3 protocols
  - Eyes open, resting
  - Eyes closed, resting
  - Eyes closed, counting
- Time-derivatives of EEG voltages were examined
EEG oscillation frequencies are associated with brain function

Frequency ranges
- δ band (0.5—3.5 Hz)
- θ band (3.5—7.5 Hz)
- α₁ band (7.5—9.5 Hz)
- α₂ band (9.5—12.5 Hz)
- β₁ band (12.5—17.5 Hz)
- β₂ band (17.5—25 Hz)
- γ band (25—40 Hz)

Brain function(s)/alertness
- Sleepy/sleep
- Sleepy/daydreaming
- Alert
- Alert
- Alert & attentive
- Alert & attentive
- Short-term memory/cross-modal tasks
26 features were computed

Spectral power features
(1) $P_\delta$: power in $\delta$ band
(2) $P_\theta$: power in $\theta$ band
(3) $P_{\alpha_1}$: power in $\alpha_1$ band
(4) $P_{\alpha_2}$: power in $\alpha_2$ band
(5) $P_{\beta_1}$: power in $\beta_1$ band
(6) $P_{\beta_2}$: power in $\beta_2$ band
(7) $P_\gamma$: power in $\gamma$ band

Relative spectral power features
(8) $P_\delta^r$: relative power in $\delta$ band
(9) $P_\theta^r$: relative power in $\theta$ band
(10) $P_{\alpha_1}^r$: relative power in $\alpha_1$ band
(11) $P_{\alpha_2}^r$: relative power in $\alpha_2$ band
(12) $P_{\beta_1}^r$: relative power in $\beta_1$ band
(13) $P_{\beta_2}^r$: relative power in $\beta_2$ band
(14) $P_\gamma^r$: relative power in $\gamma$ band

Additional spectral features
(15) $TP$: total power (0.5—40 Hz)
(16) $f_\alpha^{peak}$: peak $\alpha$ freq
(17) $f_{med}$: median freq
(18) $S_{spec}$: spectral entropy

Spectral power ratios
(19) $R_1 = \frac{P_\theta}{P_{\alpha_1} + P_{\alpha_2} + P_{\beta_1}}$
(20) $R_2 = \frac{P_\theta}{P_{\delta} + P_\theta + P_{\alpha_1} + P_{\beta_1} + P_{\beta_2}}$
(21) $R_3 = \frac{P_\theta}{P_{\alpha_1} + P_{\alpha_2}}$

Entropy & complexity features
(22) $A$: activity
(23) $M$: mobility
(24) $C$: complexity
(25) $S_{samp}$: sample entropy
(26) $C_{LZ}$: Lempel-Ziv complexity
Spectral features were calculated using spectral density

- Welch Modified Avg. Periodogram
  - 2 sec windows
  - 50% overlap
  - Hanning window (50% cosine taper)
  - Periodograms averaged for each window and time-averaged
Entropy and complexity features were time-averaged

- 5 sec windows
  - Solid lines
- 50% overlap
  - Dashed lines
- Time-averaged
  - $X_i = \text{feature for window } i, i = 1, \ldots, N$
  - $X = \frac{1}{N} \sum_{i=1}^{N} X_i$
Features were used for binary classification

- Features were calculated for each channel
- Support vector machine (SVM)
- Leave-one-out cross validation (LOOCV)
- Tested channel-averaged & individual features
  - 3 protocols
  - 30 sec, 1 min, 2 min sample lengths
  - Combinations of 1 to 4 features
Support Vector Machine (SVM)

• Collection of techniques
  – Pattern recognition
  – Nonlinear regression

• Construct hyperplane as decision surface in feature space

• Goal is to maximize margin between examples of each category
Leave-one-out cross validation (LOOCV)

• For each record
  – Generate SVM model using all other records
  – Current record tested using trained model
• Rigorous method of cross-validation
• Helps to ensure results can be generalized to other data sets
Channel-averaged feature results for 30 sec sample lengths

<table>
<thead>
<tr>
<th>Binary Test</th>
<th>Protocol 1</th>
<th>Protocol 2</th>
<th>Protocol 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCI vs. NC</td>
<td>93.6% (93.8%, 93.3%) (15), (16), (18), (24)</td>
<td>80.7% (87.5%, 73.3%) (3), (8), (10), (25)</td>
<td>87.1% (75%, 100%) (6), (10), (16), (25)</td>
</tr>
<tr>
<td>AD vs. NC</td>
<td>86.7% (86.7%, 86.7%) (14), (18), (22), (25)</td>
<td>83.3% (80%, 86.7%) (10), (12), (24), (25)</td>
<td>90% (86.7%, 93.3%) (8), (12), (18), (20)</td>
</tr>
<tr>
<td>MCI vs. AD</td>
<td>87.1% (80%, 93.8%) (1), (8), (17), (24)</td>
<td>87.1% (73.3%, 87.5%) (13), (14), (24), (25)</td>
<td>77.4% (73.3%, 81.3%) (1), (20), (20), (25)</td>
</tr>
</tbody>
</table>
### Individual channels’ feature results for MCI vs. NC

<table>
<thead>
<tr>
<th>Results</th>
<th>Channel</th>
<th>Protocol</th>
<th>Time segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>93.3% (93.8%, 86.7%) (3), (22), (24)</td>
<td>OZ</td>
<td>Eyes open</td>
<td>30 s</td>
</tr>
<tr>
<td>93.3% (93.8%, 86.7%) (6), (20), (23), (24)</td>
<td>O2</td>
<td>Eyes closed</td>
<td>1 min</td>
</tr>
<tr>
<td>87.1% (93.8%, 80%) (13), (14), (21)</td>
<td>P8</td>
<td>Eyes closed, counting</td>
<td>2 min</td>
</tr>
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</table>
## Individual channels’ feature results for AD vs. NC

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<tr>
<td>93.3% (93.3%, 93.3%) (10), (12), (17), (23)</td>
<td>OZ</td>
<td>Eyes closed, counting</td>
<td>1 min</td>
</tr>
<tr>
<td>90% (80%, 100%) (6), (12), (19), (22)</td>
<td>O2</td>
<td>Eyes closed, counting</td>
<td>30 s</td>
</tr>
<tr>
<td>90% (86.7%, 93.3%) (2), (12), (22)</td>
<td>OZ</td>
<td>Eyes closed, counting</td>
<td>30 s</td>
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</tbody>
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## Individual channels’ feature results for MCI vs. AD

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<tr>
<td>93.6% (93.3%, 93.8%) (1), (18), (23), (24)</td>
<td>PZ</td>
<td>Eyes closed, counting</td>
<td>2 min</td>
</tr>
<tr>
<td>90.3% (93.3%, 87.5%) (3), (6), (21), (24)</td>
<td>O1</td>
<td>Eyes open</td>
<td>2 min</td>
</tr>
<tr>
<td>90.3% (86.7%, 93.8%) (5), (12), (18), (23)</td>
<td>OZ</td>
<td>Eyes closed</td>
<td>2 min</td>
</tr>
</tbody>
</table>
Monte Carlo simulations were used to estimate p-value of results

- 30 subjects
  - 15 “normal”
  - 15 “abnormal”
- Random features
  - Uniform dist.
- Tested combinations of 1 to 4 features
- P-values
  - 0.0514 (87%, 4 features)
  - 0.00589 (90%, 4 features)
Future work will include additional features, data reduction, etc.

• Additional features
  – Wavelet analyses
  – Dipole source localization modeling
  – Synchronization measures

• 3-way discrimination

• Efficient feature selection

• Data reduction (features & channels)
Acknowledgements

• Financial support: NSF, ORNL, UKY
• Collaborators:
  – Xiaopeng Zhao (UTK, Advisor)
  – Nancy Munro (ORNL)
  – Yang Jiang (UKY)
“The scientist is not a person who gives the right answers, he’s one who asks the right questions” – Claude Lévi-Strauss

- $A = \sigma_0$
- $M = \sqrt{\frac{\sigma_1}{\sigma_0}}$
- $C = \sqrt{\frac{\sigma_2}{\sigma_1} - \frac{\sigma_1}{\sigma_0}}$
- $S_{spec} = -\sum_{i=1}^{k} p(f_i) \ln p(f_i) \approx -\sum_{i=1}^{k} \frac{P(f_i)}{TP} \ln \left(\frac{P(f_i)}{TP}\right)$