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

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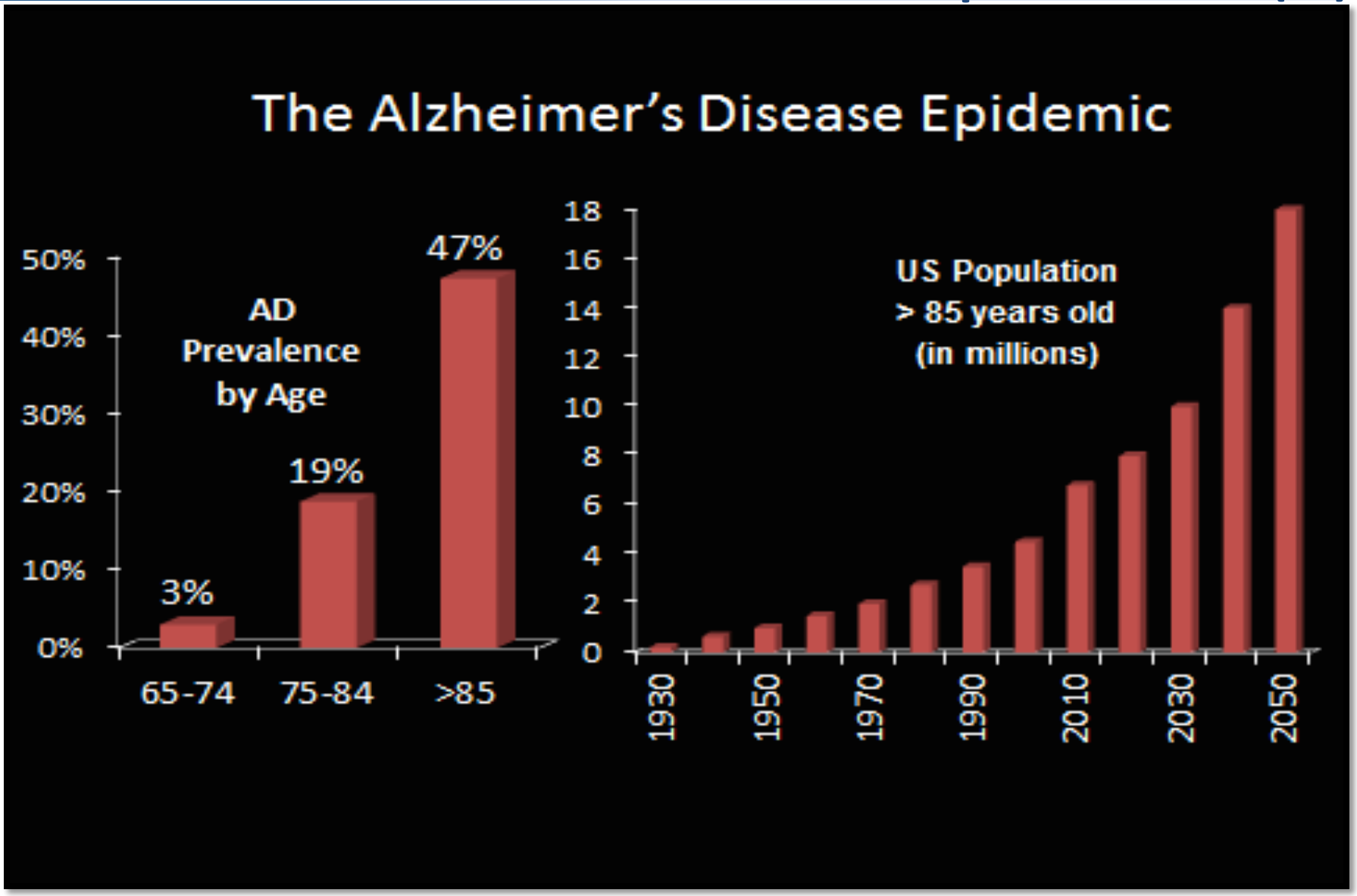
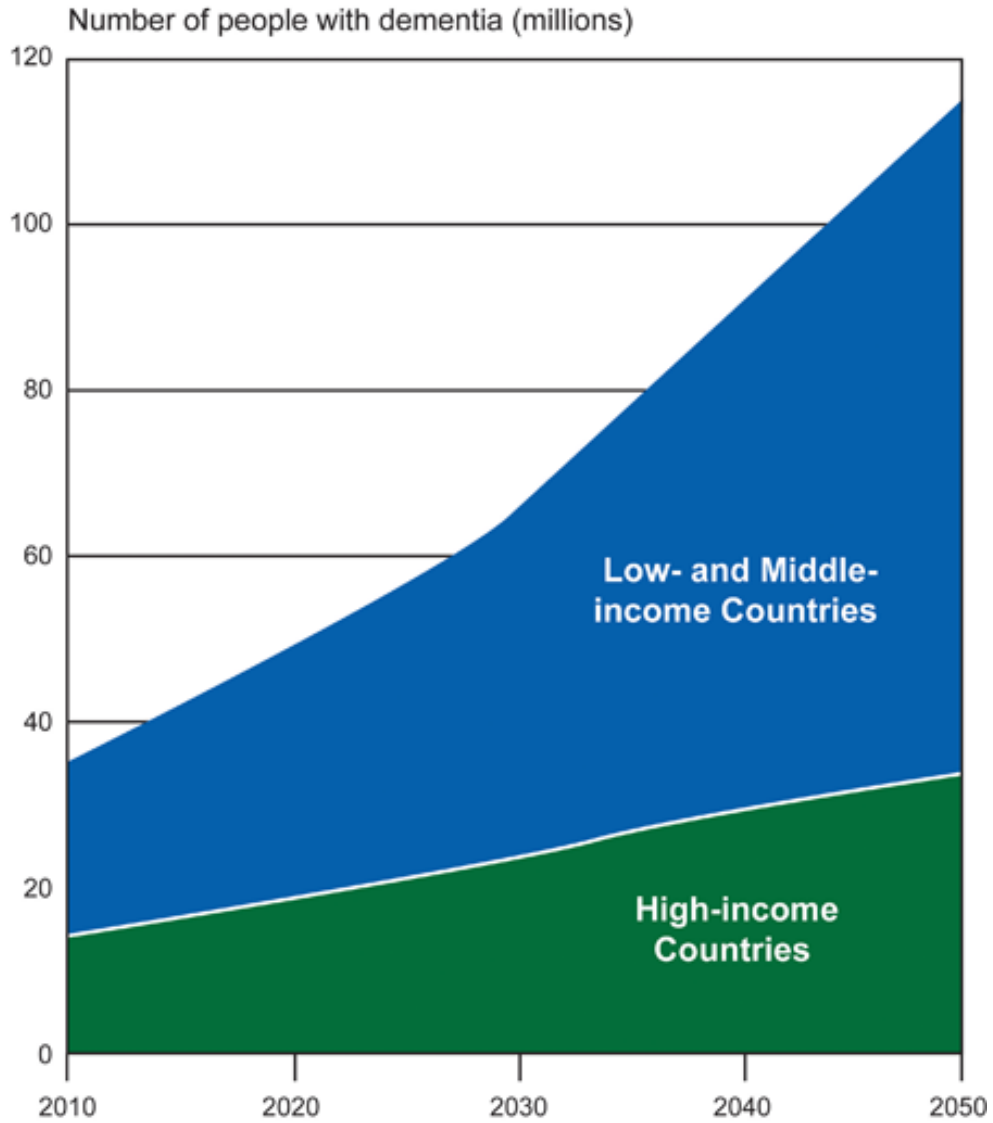
Presentation Overview

- Preamble on Alzheimer's Disease (AD)
- Existing diagnostic tools
- Drawbacks and motivation for EEG
- Where are we now
- Where we are heading
- Conclusions

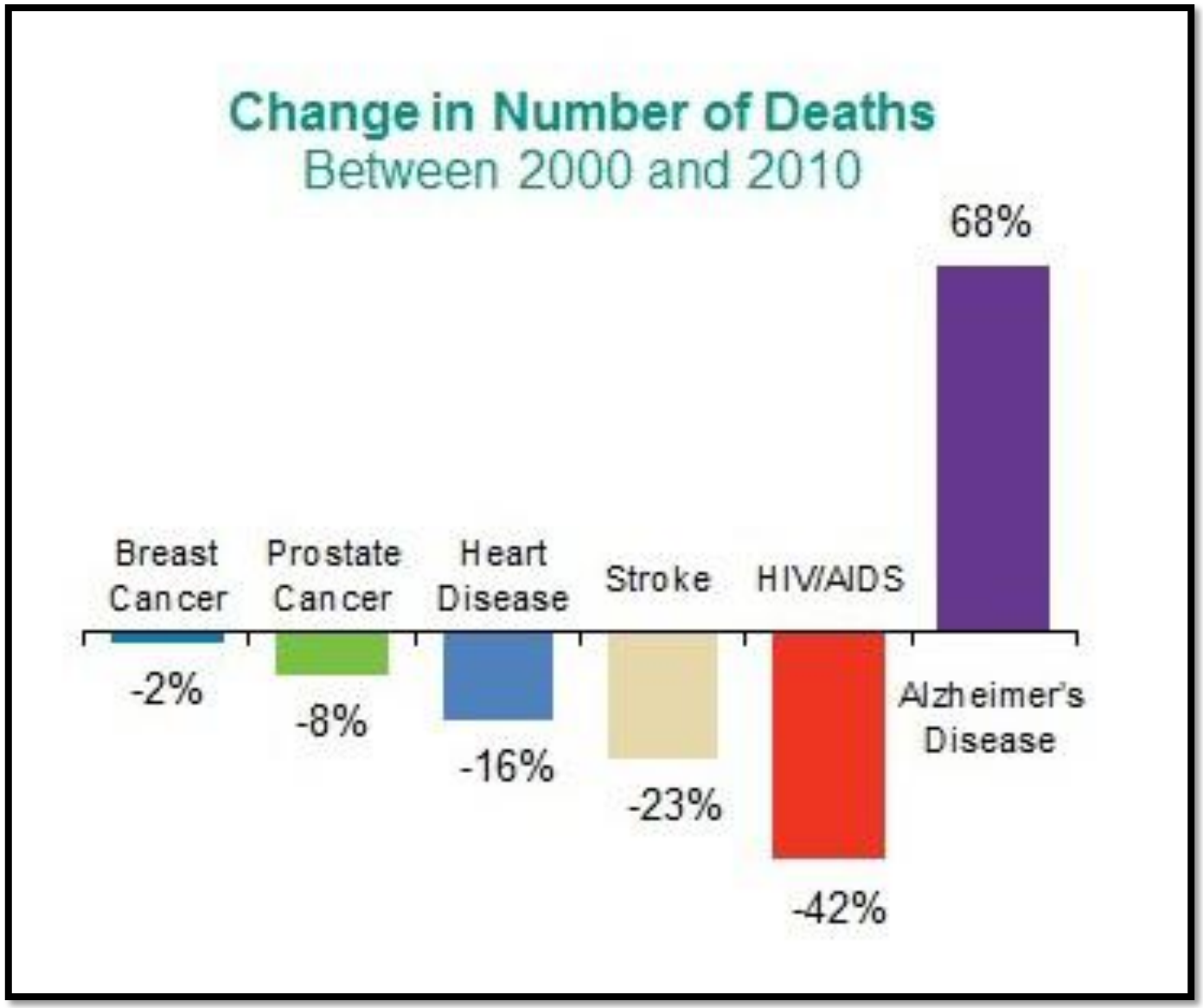
Alzheimer's Disease: An Epidemic (?)



Worldwide Epidemic



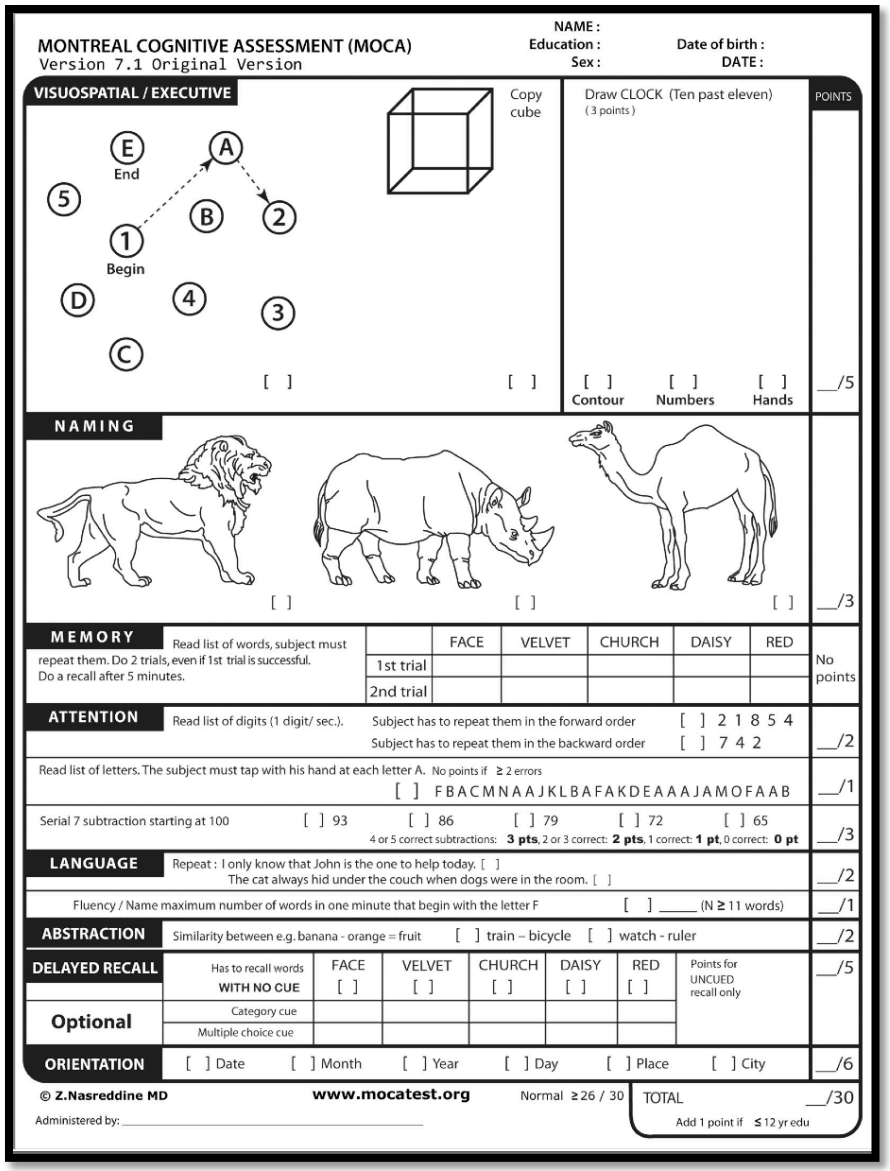
Change in Number of Deaths



Something Needs to be Done

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



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE — Copy cube — Draw CLOCK (Ten past eleven) (3 points) — POINTS

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C

[ ] [ ] Contour [ ] Numbers [ ] Hands __/5

NAMING __/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4 — Subject has to repeat them in the backward order [ ] 7 4 2 __/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B __/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** __/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] __/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) __/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler __/2

DELAYED RECALL

	FACE	VELVET	CHURCH	DAISY	RED	
Has to recall words WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]	Points for UNCUED recall only
Optional Category cue						
Optional Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City __/6

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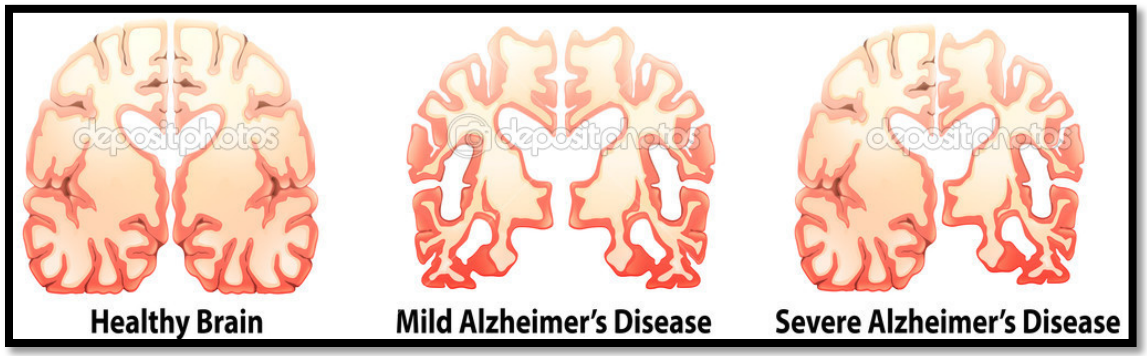
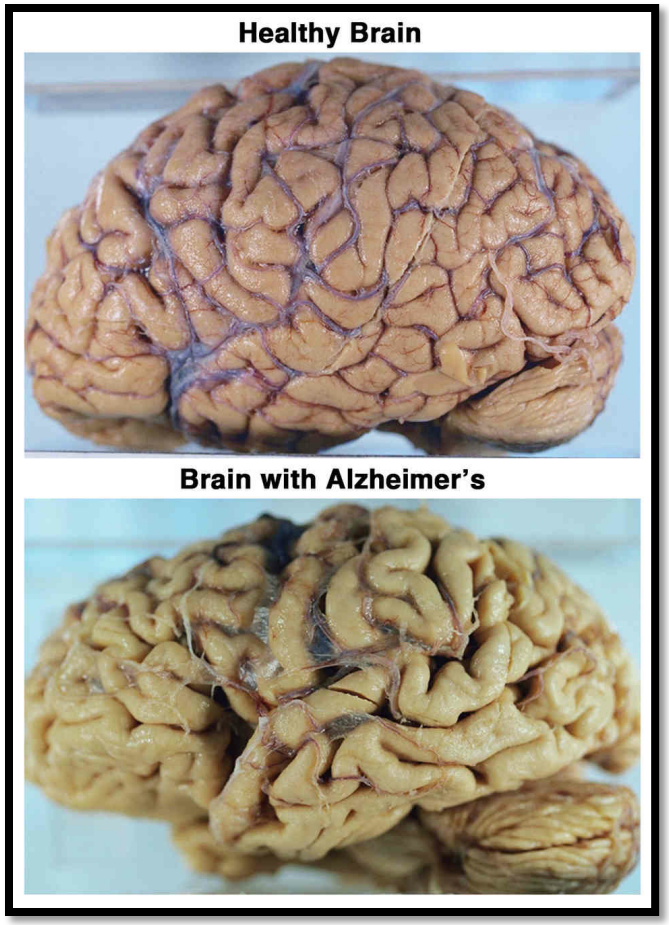
TOTAL __/30
Add 1 point if ≤ 12 yr edu

Administered by: _____

Definite Diagnosis

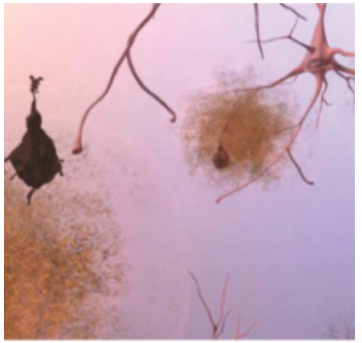
- Definite diagnosis requires post-mortem histopatho-logical analysis of the brain

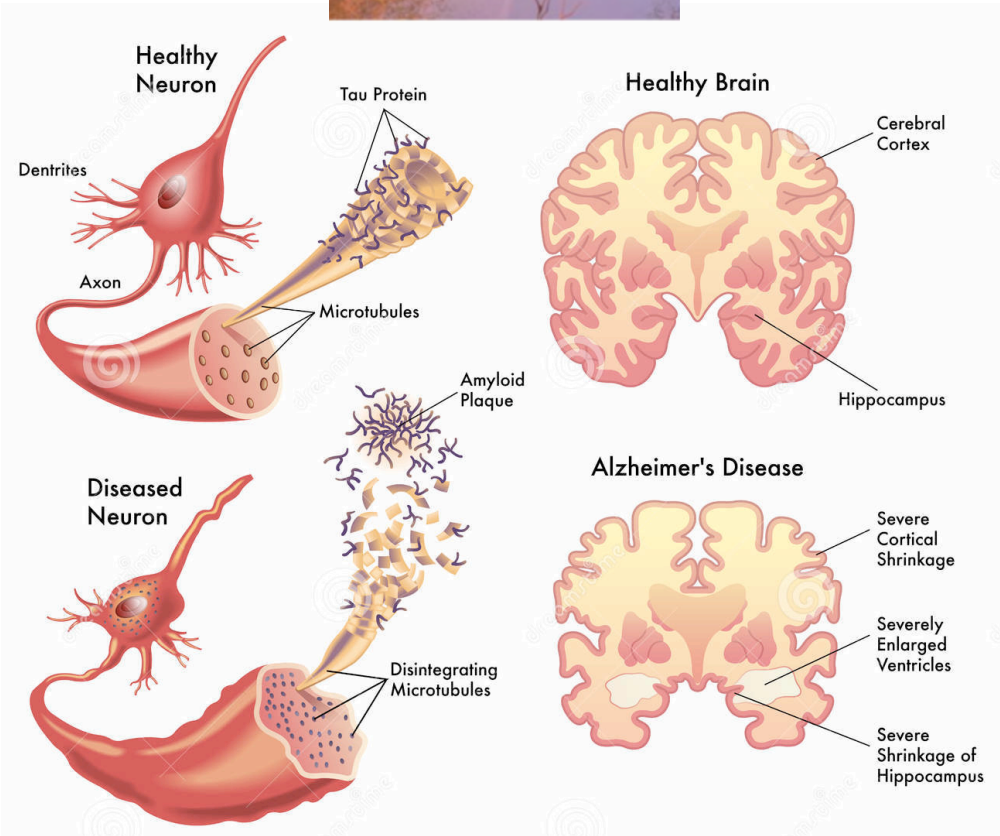




What is Known

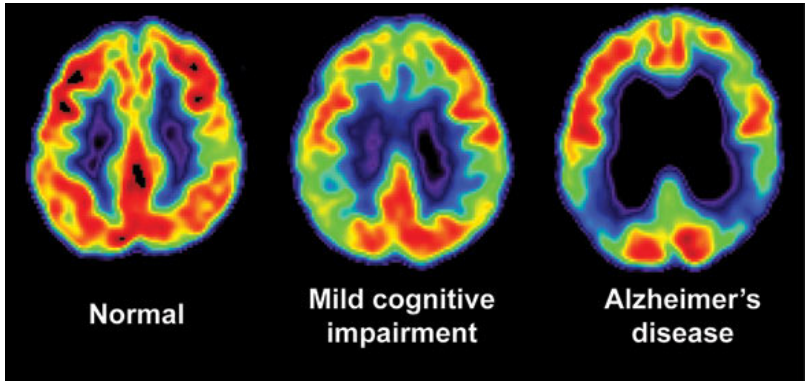
- Beta amyloid plaques
  - "Sticky" protein fragments that are normally broken down and eliminated
  - AD: block cell signaling and blood flow
- Neurofibrillary tangles
  - Microtubule transports nutrients through nerve cell → tau protein abnormal with AD

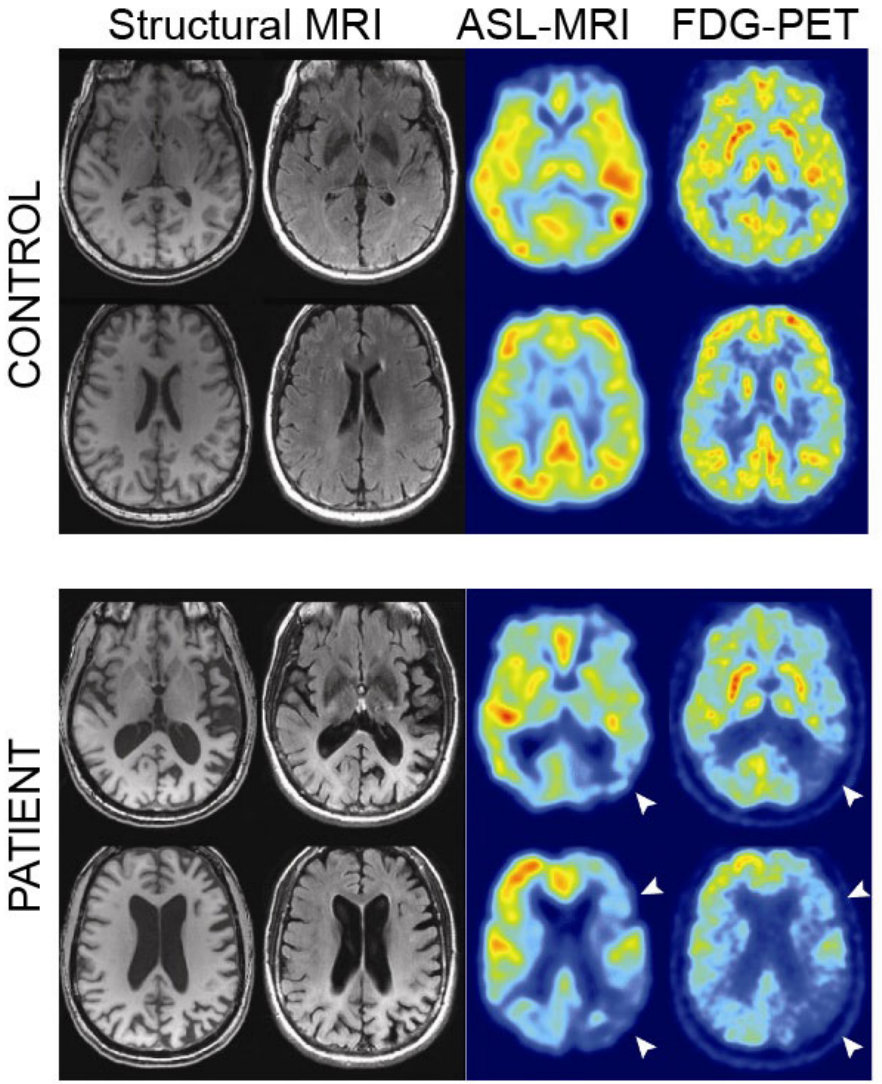




How is Technology Helping?

- S-MRI: detect tissue loss
- PET: tracer binds to beta amyloid
- SPECT perfusion: assess regional blood flow





Drawbacks & Motivation for EEG

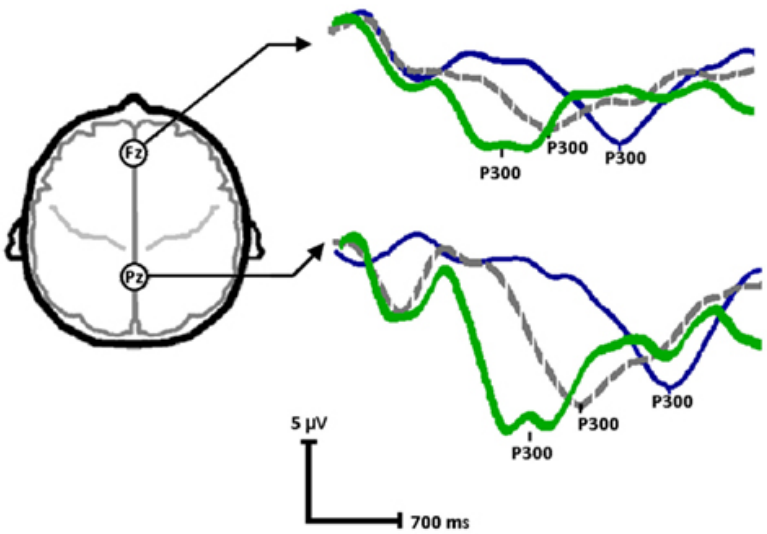
- Tissue loss and atrophies represent late stage of neural dysfunction → early detection (?!?)
- Expensive equipment, experienced personnel
  - Low-income countries, rural and remote areas (?!?)
  - Urban areas: long waiting times (e.g., in Canada: up to 6 months for non-emergency MRI)
- EEG: better 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

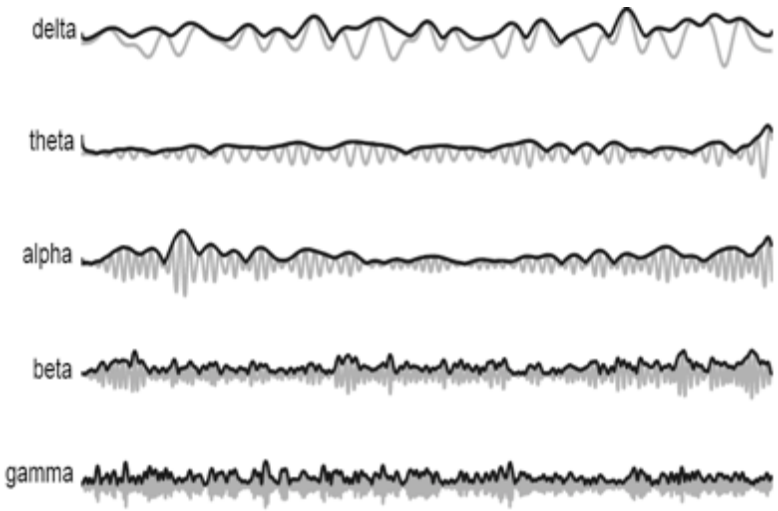
ERP's

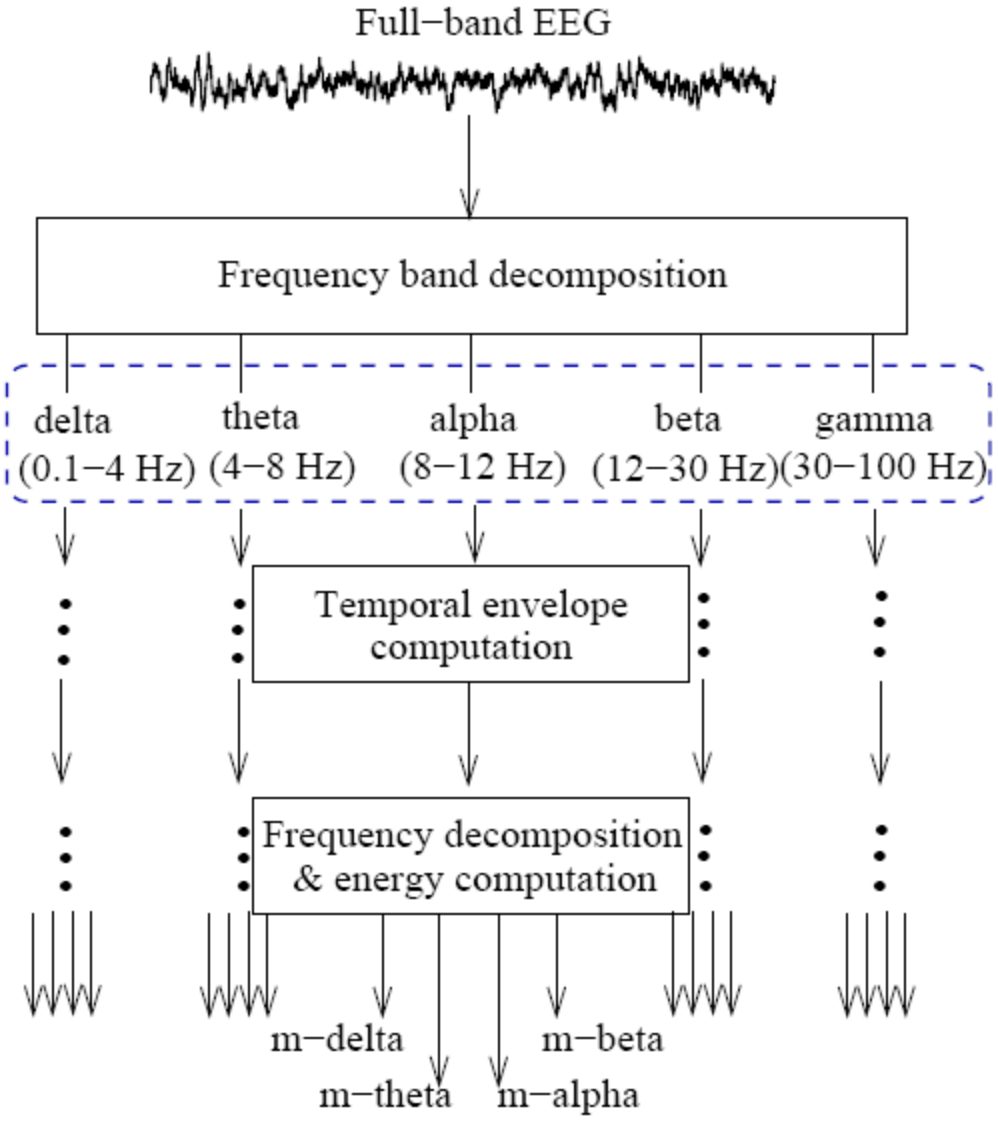


	Lat P300 Fz	Amp P300 Fz	Lat P300 Pz	Amp P300 Pz
Controls	431.78 (21.3)	5.69 (1.85)	445.13 (27.3)	7.20 (3.25)
MCI	537.48 (60.7)	3.50 (1.42)	528.94 (73.4)	4.51 (1.61)
AD	564.31 (6.1)	3.13 (1.59)	568.37 (77.4)	5.24 (1.74)

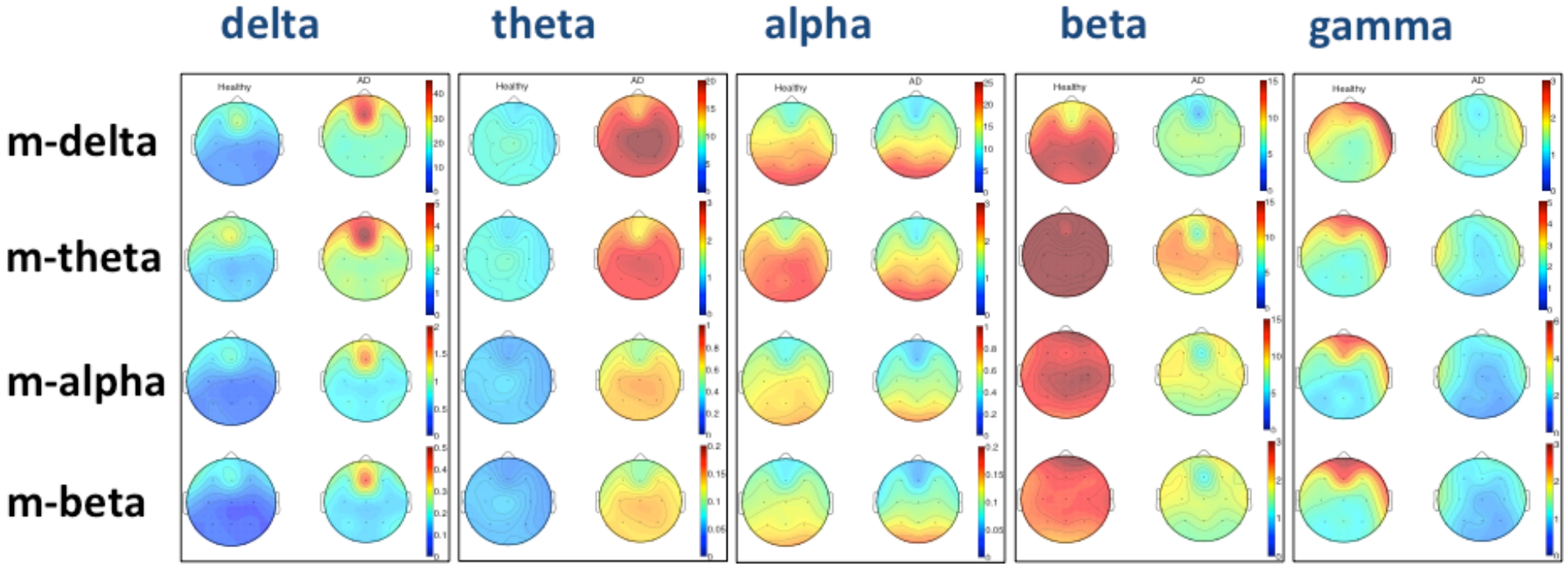
New EEG Features

Hemodynamics involved in information processing via neural activity **modulation**





Healthy vs. Alzheimer's



Experimental Results (22:AD, 12:C)

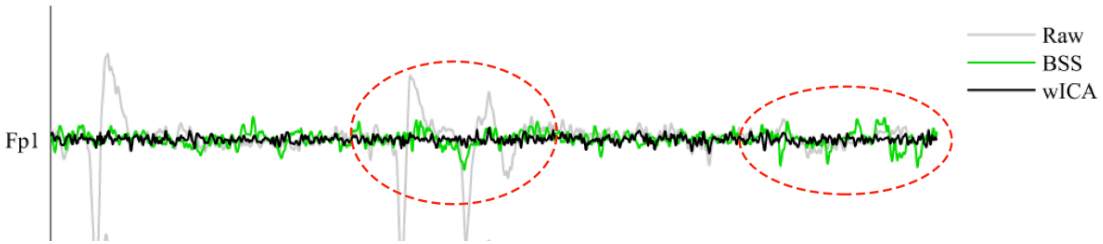
Feature	Accuracy (%)	Sensitivity (%)	Specificity (%)
Coherence (I)	70.6	86.4	41.7
Power (II)	85.3	90.9	75.0
PME (III)	88.4	90.9	83.3
I + III	79.4	86.4	66.7
II + III	***94.1***	***96.5***	***91.7***
I + II + III	91.2	96.5	83.3

(Not) Automated and (Not) Portable

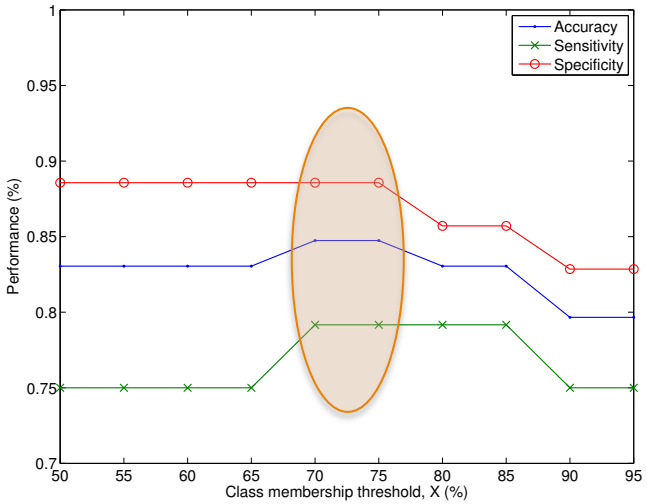
- Multi-channel medical (research) grade EEG
  - 20, 32, 64 channels
  - **Not portable**
- Require visual inspection of artifact-free epochs
  - Remove movement, muscle, eye-blink artifacts
  - Labor-intensive, requires experienced personnel
  - **Not automated**

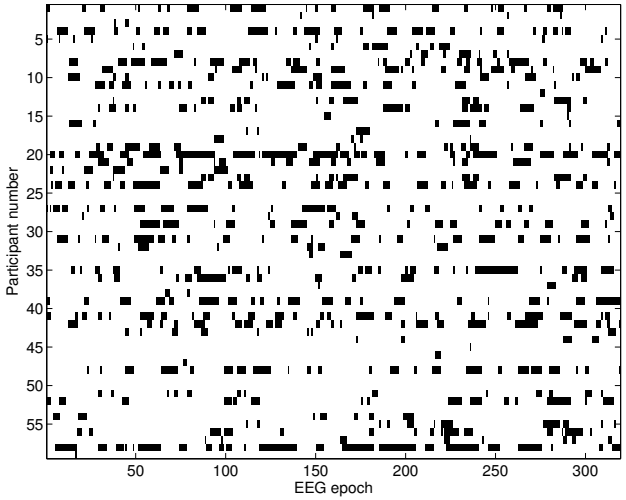
Automated and Portable

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



- Relevance vector machine (RVM) vs SVM





Experimental Results

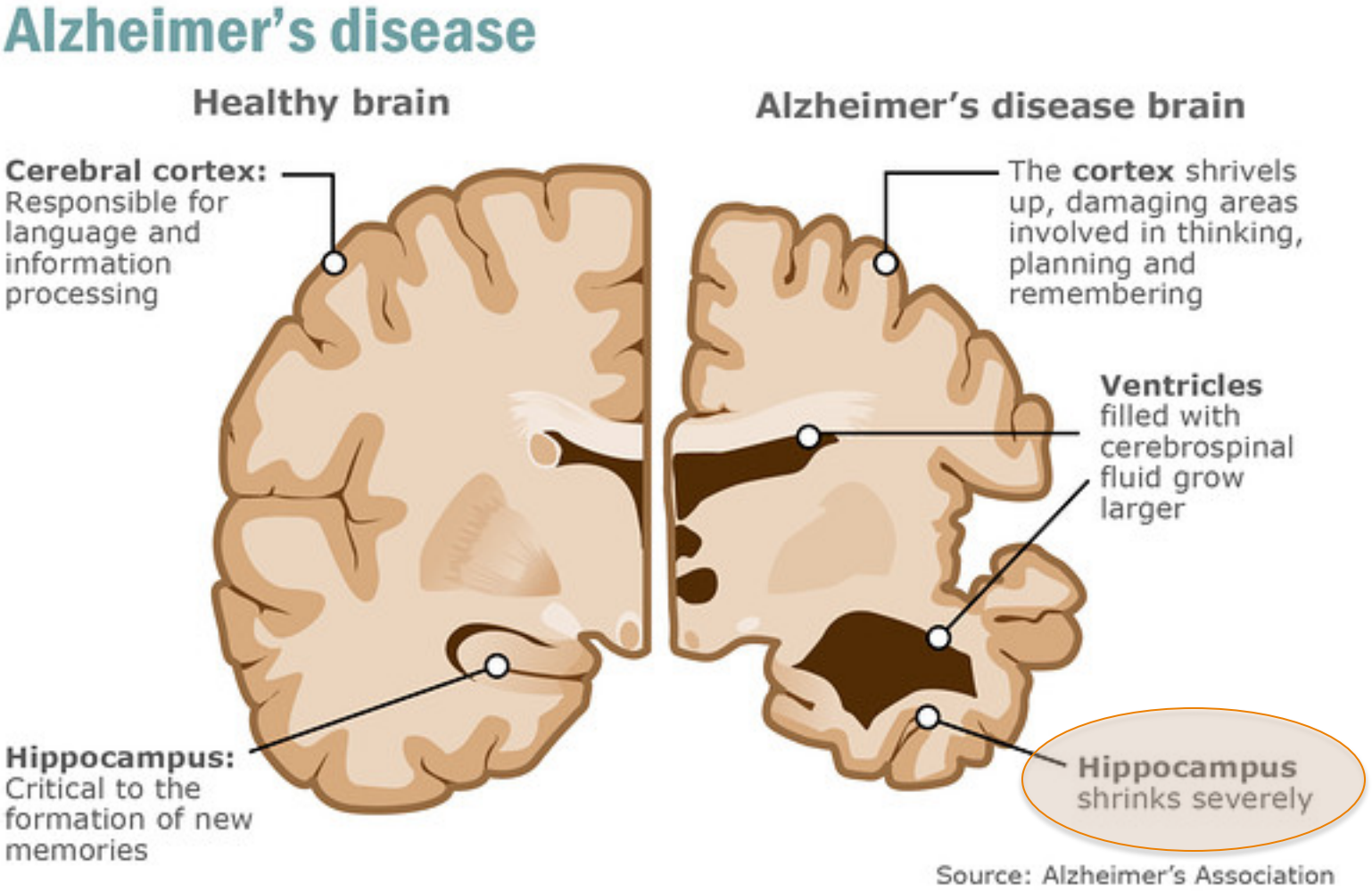
- 35 AD, 24 C
- Benchmark: visual inspection + SVM

System	Accuracy (%)	Sensitivity (%)	Specificity (%)
Benchmark	84.7	75.0	91.4
SVM	81.4	75.0	85.7
RVM	84.7	79.2	88.6

- Advantages over visual inspection:
  - Improved sensitivity relative to benchmark
  - Information from **frontal** electrodes kept

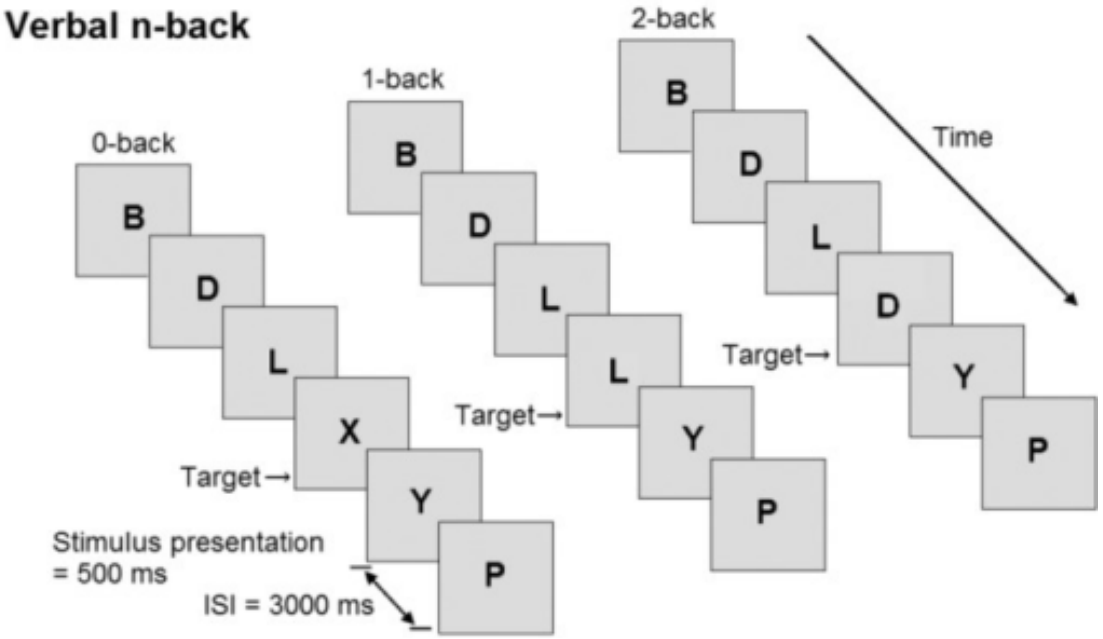

WHAT NEXT?
DON'T TELL ME.

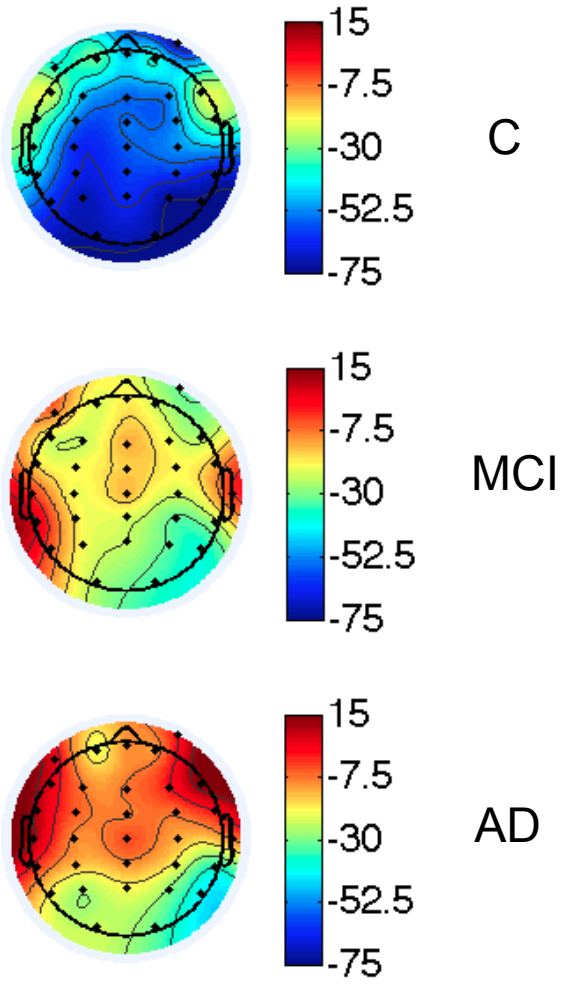
Resting-Awake vs Mental Activity



Hippocampal Activation

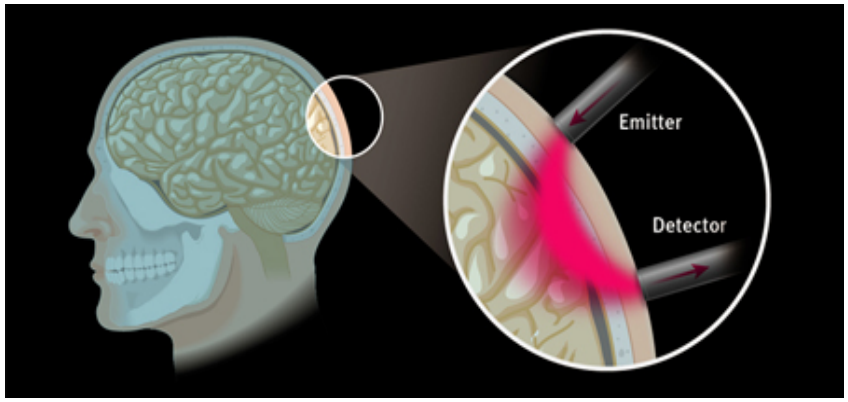
- Working memory
- ERD/ERS

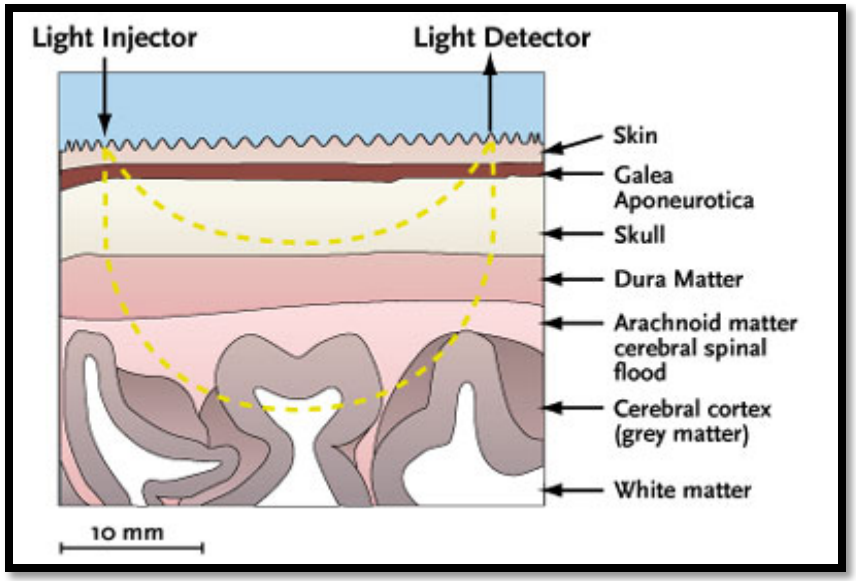


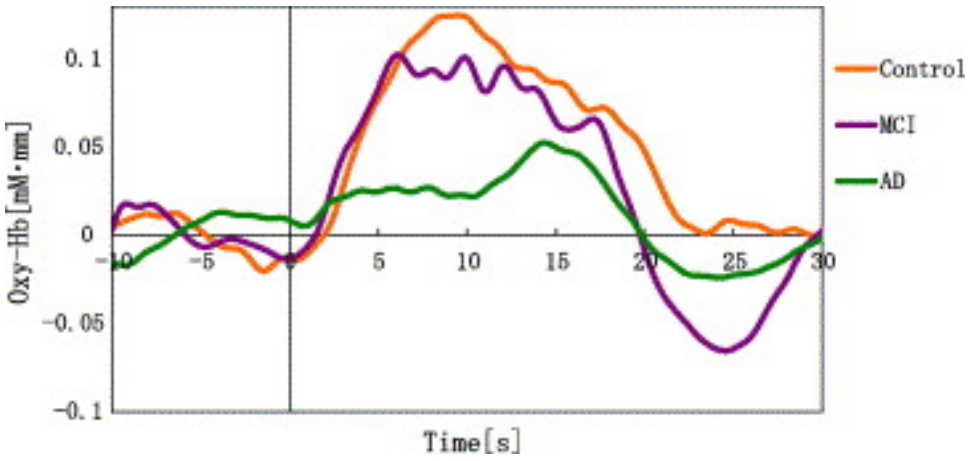


Multimodal Neuroimaging

- 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

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  - Francisco Fraga, UFABC, Brazil
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Questions?

"If the brain were so simple we could understand it, we would be so simple we couldn't"

- Lyall Watson