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EEG-based feature extraction, selection and classification for Alzheimer's disease early diagnosis support

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Abstract

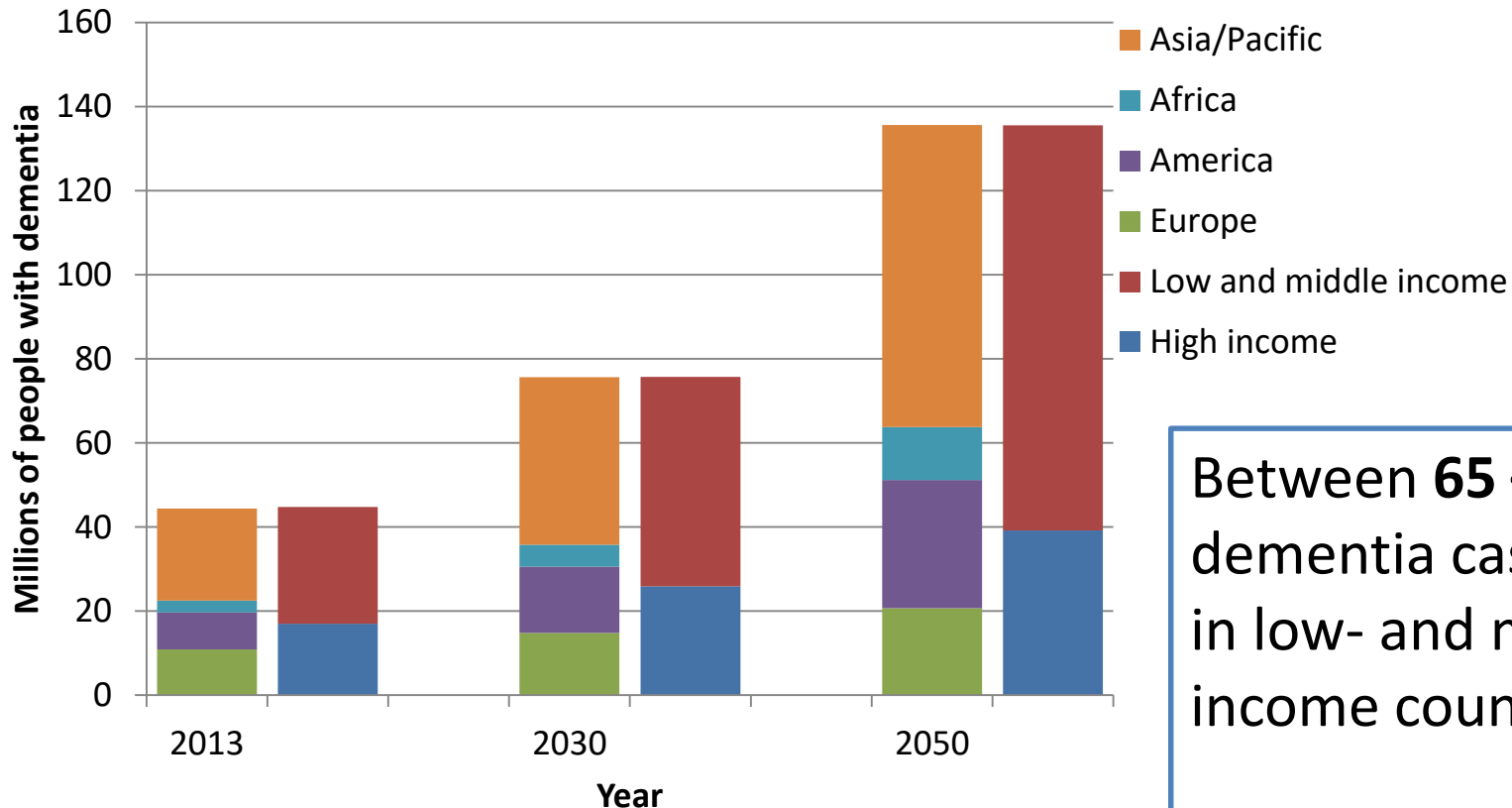
This talk is a summary of my research over the last ten years on the topic of EEG processing and classification to support early diagnosis of Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI), which is an intermediate state between healthy aging and the dementia caused by AD. It is very important to properly diagnose and follow patients with MCI since they are a group at risk of developing dementia and may or may not evolve to AD. Although AD is progressive and so far an incurable disease, early diagnosis is crucial to introduce medication and treatment that can delay the disease progression and improve the quality of life of MCI and AD patients.

Current research partners in AD-EEG

- **Dr. Renato Anghinah (since 2009)**
 - FMUSP, research group of Prof. Ricardo Nitrini (coauthor of the study on cover of latest *Pesquisa FAPESP* magazine)
- **Prof. Tiago H. Falk (since 2010)**
 - INRS-EMT, University of Quebec, Montreal, Canada
- **Profa. Ruth F. Santos-Galduroz (since 2011)**
 - *Biociências* UNESP, Rio Claro, SP
- **Profa. Natalie A. Philips (since 2012)**
 - Psychology, Concordia University, Montreal, Canada
- **Profa. Marcia Regina Cominetti (since 2018)**
 - *Gerontologia* UFSCar, São Carlos, SP
- **Prof. Claudio Babiloni (since 2019)**
 - Human Physiology, Sapienza University of Rome, Italy

Dementia and AD incidence

- Dementia
- Alzheimer's disease (AD) accounts for 60-80% of dementia cases worldwide



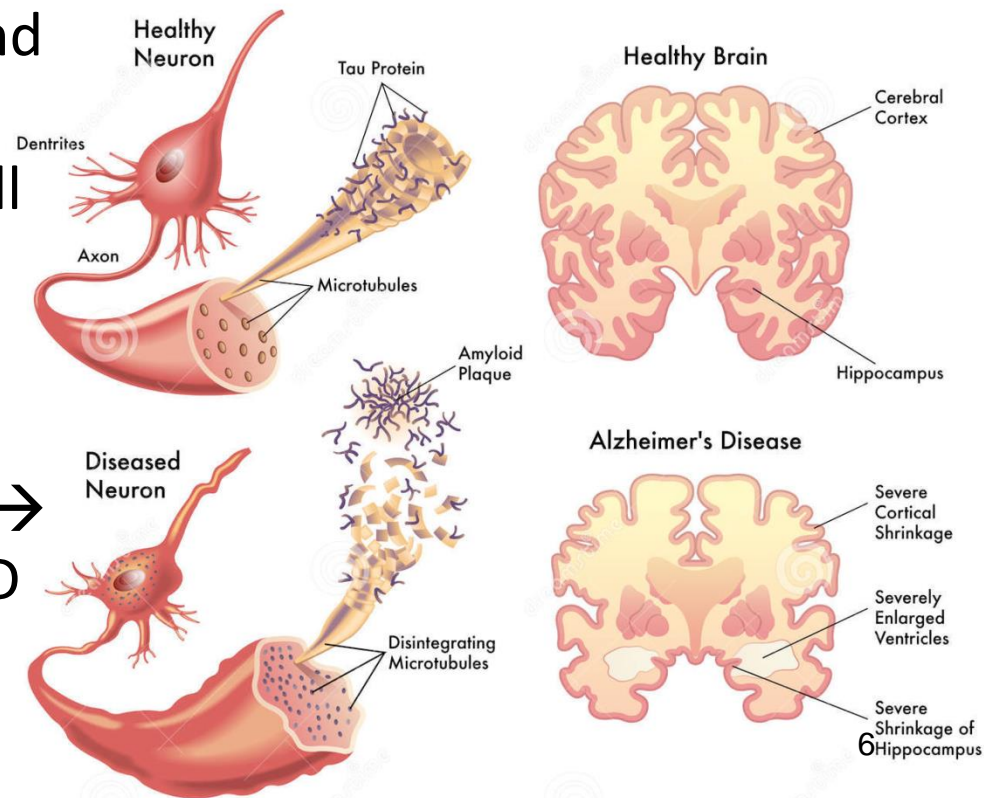
Between **65 – 70%** of dementia cases are in low- and middle-income countries

Need for early diagnosis



Pathophysiological biomarkers

- CSF biomarkers and amyloid PET
- Beta amyloid plaques
 - “Sticky” protein fragments that are normally broken down and eliminated
 - AD: accumulate and block cell signaling/blood flow
- Neurofibrillary tangles
 - Microtubule transports nutrients through nerve cell → tau protein abnormal with AD causes their collapse



EEG-based topographical markers

- CSF, PET and fMRI: Invasive, expensive equipment
 - Low-income countries, rural and remote areas (?!?)
- EEG: Non-invasive, less expensive equipment
 - could be better suited to reveal functional impairment as it reflects the electrical activity of neural tissue

Classical AD/MCI-EEG Findings

Resting-state EEG

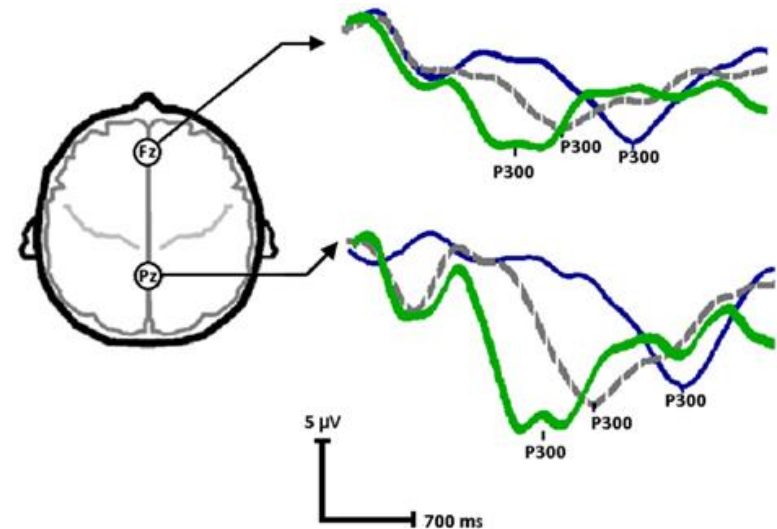
Resting-awake, eyes-closed

- “Slowing” of the EEG: increase in EEG low-frequency power and decrease in alpha/beta
- Inter-hemispheric disconnect (alpha/beta)
- Non-linear dynamics: decrease in complexity

Task-oriented EEG

ERP's – P300

- P300: lower amplitude, longer latency



	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)

Resting-state or Task-oriented AD-EEG?

- Which one is better for early AD diagnosis support: Resting-state or Task-oriented EEG?
- Advantages of resting-state EEG:
 - Default Mode Network (DMN) disrupted in AD
 - Difficulty for AD patients to perform tasks
- Advantages of task-oriented EEG:
 - Memory and cognitive decline in AD
 - Focus on MCI patients (early diagnosis)

Our AD/MCI-EEG Findings

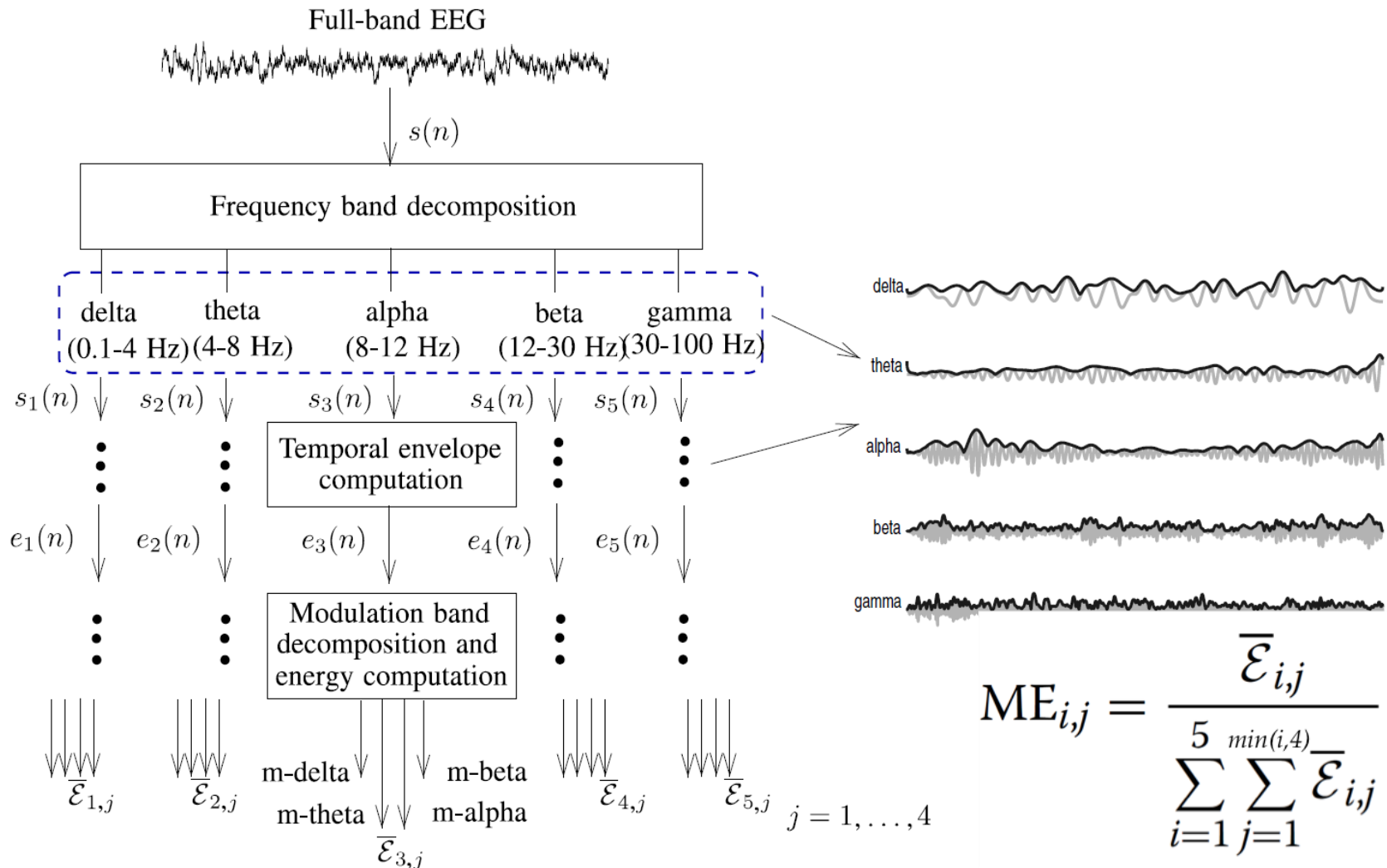
- We (I and my research partners) used both resting-state and task-oriented AD-EEG
- **My view on EEG processing research:**
 1. First you go to **traditional** techniques
 2. After, you can go to **novel** techniques

“Traditional” resting-state AD-EEG publications

TITLE	CITED BY	YEAR
Improving Alzheimer's disease diagnosis with machine learning techniques LR Trambaiolli, AC Lorena, FJ Fraga, PAM Kanda, R Anghinah, R Nitrini Clinical EEG and neuroscience 42 (3), 160-165	52	2011
Clinician's road map to wavelet EEG as an Alzheimer's disease biomarker PAM Kanda, LR Trambaiolli, AC Lorena, FJ Fraga, LFI Basile, R Nitrini, ... Clinical EEG and neuroscience 45 (2), 104-112	15	2014
Does EEG montage influence Alzheimer's disease electroclinic diagnosis? LR Trambaiolli, AC Lorena, FJ Fraga, P Kanda, R Nitrini, R Anghinah International Journal of Alzheimer's Disease 2011	15	2011
EEG epochs with less alpha rhythm improve discrimination of mild Alzheimer's PAM Kanda, EF Oliveira, FJ Fraga computer methods and programs in biomedicine 138, 13-22	8	2017
Systematic review on resting-state EEG for Alzheimer's disease diagnosis and progression assessment R Cassani, M Estarellas, R San-Martin, FJ Fraga, TH Falk Disease markers 2018	6	2018
Comparative analysis of the electroencephalogram in patients with Alzheimer's disease, diffuse axonal injury patients and healthy controls using LORETA analysis JN Ianof, FJ Fraga, LA Ferreira, RT Ramos, JLC Demario, R Baratho, ... Dementia & neuropsychologia 11 (2), 176-185	5	2017

Novel resting-state AD-EEG technique

Amplitude Modulation Features



$ME_{i,j}$: Percentage energy of **band i** modulated by **band j** $i \geq j$

AD-EEG amplitude modulation publications

TITLE	CITED BY	YEAR
Characterizing Alzheimer's disease severity via resting-awake EEG amplitude modulation analysis FJ Fraga, TH Falk, PAM Kanda, R Anghinah PLoS One 8 (8), e72240	49	2013
The effects of automated artifact removal algorithms on electroencephalography-based Alzheimer's disease diagnosis R Cassani, TH Falk, FJ Fraga, PAM Kanda, R Anghinah Frontiers in aging neuroscience 6, 55	40	2014
EEG Amplitude Modulation Analysis for Semi-Automated Diagnosis of Alzheimer's Disease TH Falk, FJ Fraga, L Trambaiolli, R Anghinah EURASIP Journal on Advances in Signal Processing, 192	37	2012
EEG spectro-temporal modulation energy: a new feature for automated diagnosis of Alzheimer's disease LR Trambaiolli, TH Falk, FJ Fraga, R Anghinah, AC Lorena 2011 Annual International Conference of the IEEE Engineering in Medicine and ...	21	2011
Towards automated electroencephalography-based Alzheimer's disease diagnosis using portable low-density devices R Cassani, TH Falk, FJ Fraga, M Cecchi, DK Moore, R Anghinah Biomedical Signal Processing and Control 33, 261-271	10	2017
Towards automated EEG-Based Alzheimer's disease diagnosis using relevance vector machines R Cassani, TH Falk, FJ Fraga, PA Kanda, R Anghinah 5th ISSNIP-IEEE Biosignals and Biorobotics Conference (2014): Biosignals and ...	10	2014
Towards an EEG-based biomarker for Alzheimer's disease: Improving amplitude modulation analysis features FJ Fraga, TH Falk, LR Trambaiolli, EF Oliveira, WHL Pinaya, PAM Kanda, ... 2013 IEEE International Conference on Acoustics, Speech and Signal ...	10	2013

“Traditional” task-oriented AD-EEG publications

TITLE	CITED BY	YEAR
P300 latency and amplitude in Alzheimer's disease: a systematic review RV Pedroso, FJ Fraga, DI Corazza, CAA Andreatto, FGM Coelho, ... Brazilian journal of otorhinolaryngology 78 (4), 126-132	46	2012
Effects of physical activity on the P 300 component in elderly people: a systematic review RV Pedroso, FJ Fraga, C Ayán, JM Cancela Carral, L Scarpari, ... Psychogeriatrics 17 (6), 479-487	8	2017
On the use of the P300 as a tool for cognitive processing assessment in healthy aging: a review SCI Pavarini, AG Brigola, BM Luchesi, ÉN Souza, ES Rossetti, FJ Fraga, ... Dementia & neuropsychologia 12 (1), 1-11	7	2018
Event-related synchronisation responses to N-back memory tasks discriminate between healthy ageing, mild cognitive impairment, and mild Alzheimer's disease FJ Fraga, LA Ferreira, TH Falk, E Johns, ND Phillips 2017 IEEE International Conference on Acoustics, Speech and Signal ...	4	2017
Early diagnosis of mild cognitive impairment and Alzheimer's with event-related potentials and event-related desynchronization in N-back working memory tasks FJ Fraga, GQ Mamani, E Johns, G Tavares, TH Falk, NA Phillips Computer methods and programs in biomedicine 164, 1-13	4	2018
EEG-based biomarkers on working memory tasks for early diagnosis of Alzheimer's disease and mild cognitive impairment GQ Mamani, FJ Fraga, G Tavares, E Johns, ND Phillips 2017 IEEE Healthcare Innovations and Point of Care Technologies (HI-POCT ...	2	2017
Effects of Physical Exercise on the P300 of Elderly With Alzheimer's Disease RV Pedroso, JM Cancela, C Ayán, AM Stein, G Fuzaro, JLR Costa, ... Journal of Physical Activity and Health 15 (6), 403-410		2018

“Traditional” task-oriented AD-EEG

TITLE	CITED BY	YEAR
Early diagnosis of mild cognitive impairment and Alzheimer’s with event-related potentials and event-related desynchronization in N-back working memory tasks FJ Fraga, GQ Mamani, E Johns, G Tavares, TH Falk, NA Phillips Computer methods and programs in biomedicine 164, 1-13	4	2018



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Early diagnosis of mild cognitive impairment and Alzheimer’s with event-related potentials and event-related desynchronization in N-back working memory tasks



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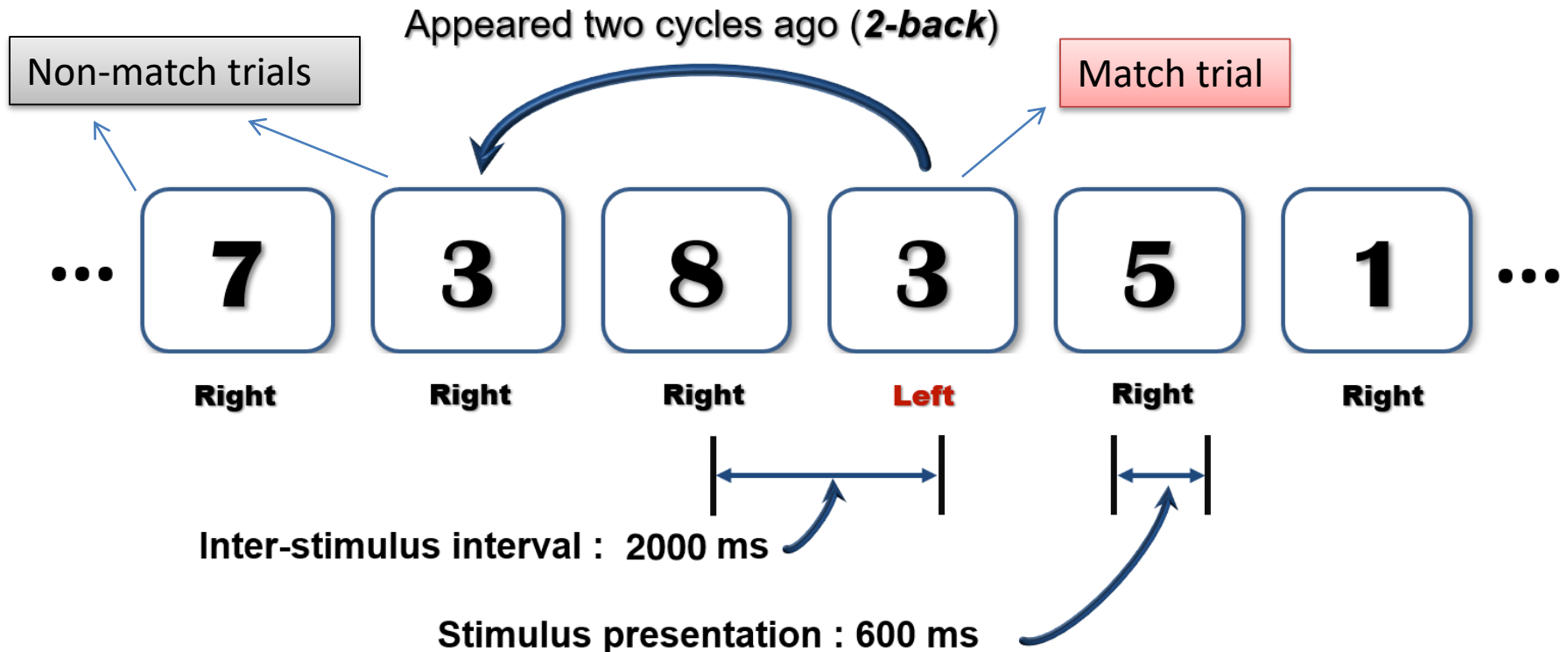
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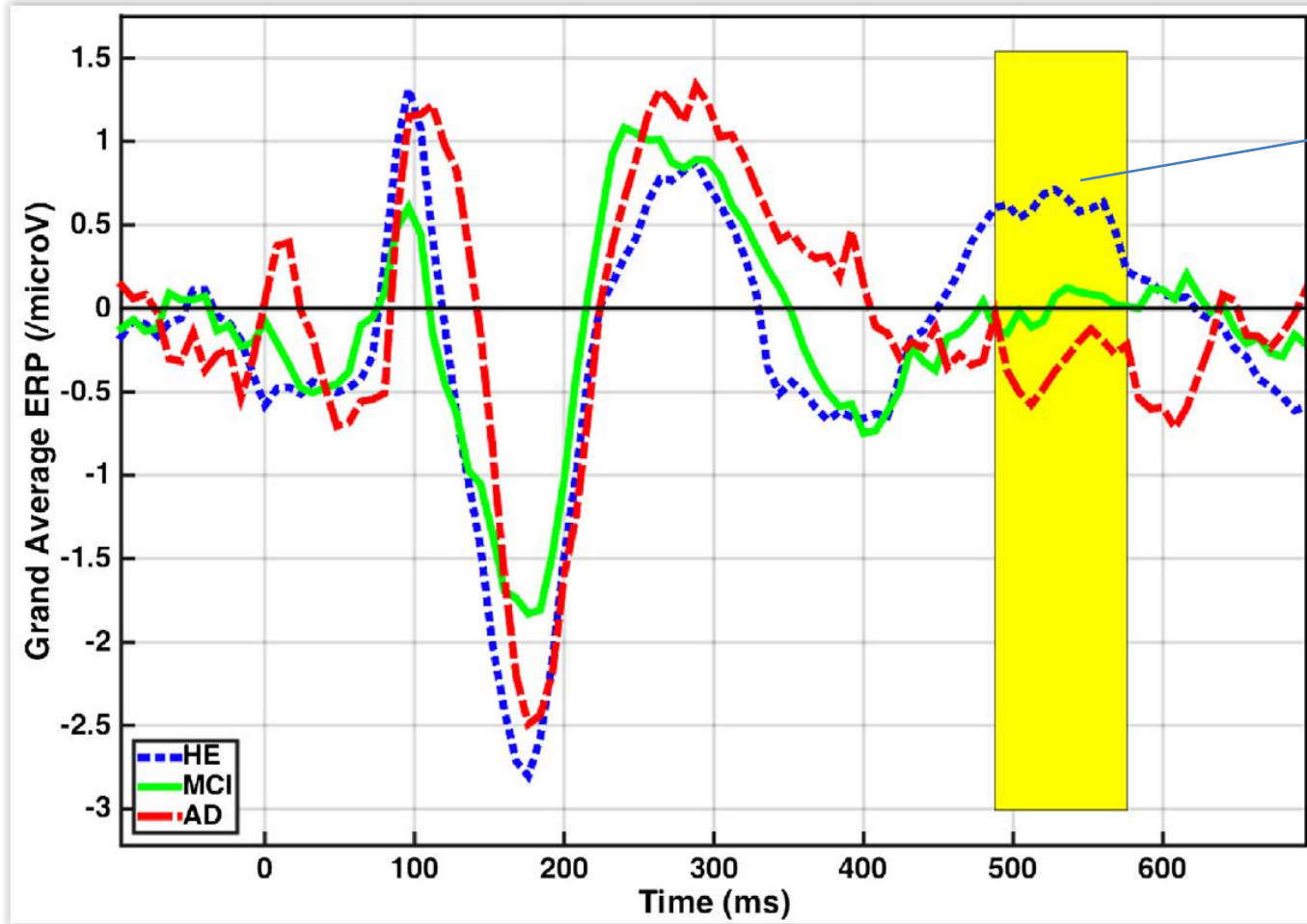
ABSTRACT

Background and Objective: In this study we investigate whether or not event-related potentials (ERP) and/or event-related (de)synchronization (ERD/ERS) can be used to differentiate between 27 healthy elderly (HE), 21 subjects diagnosed with mild cognitive impairment (MCI) and 15 mild Alzheimer’s disease (AD) patients.

N-back working memory task



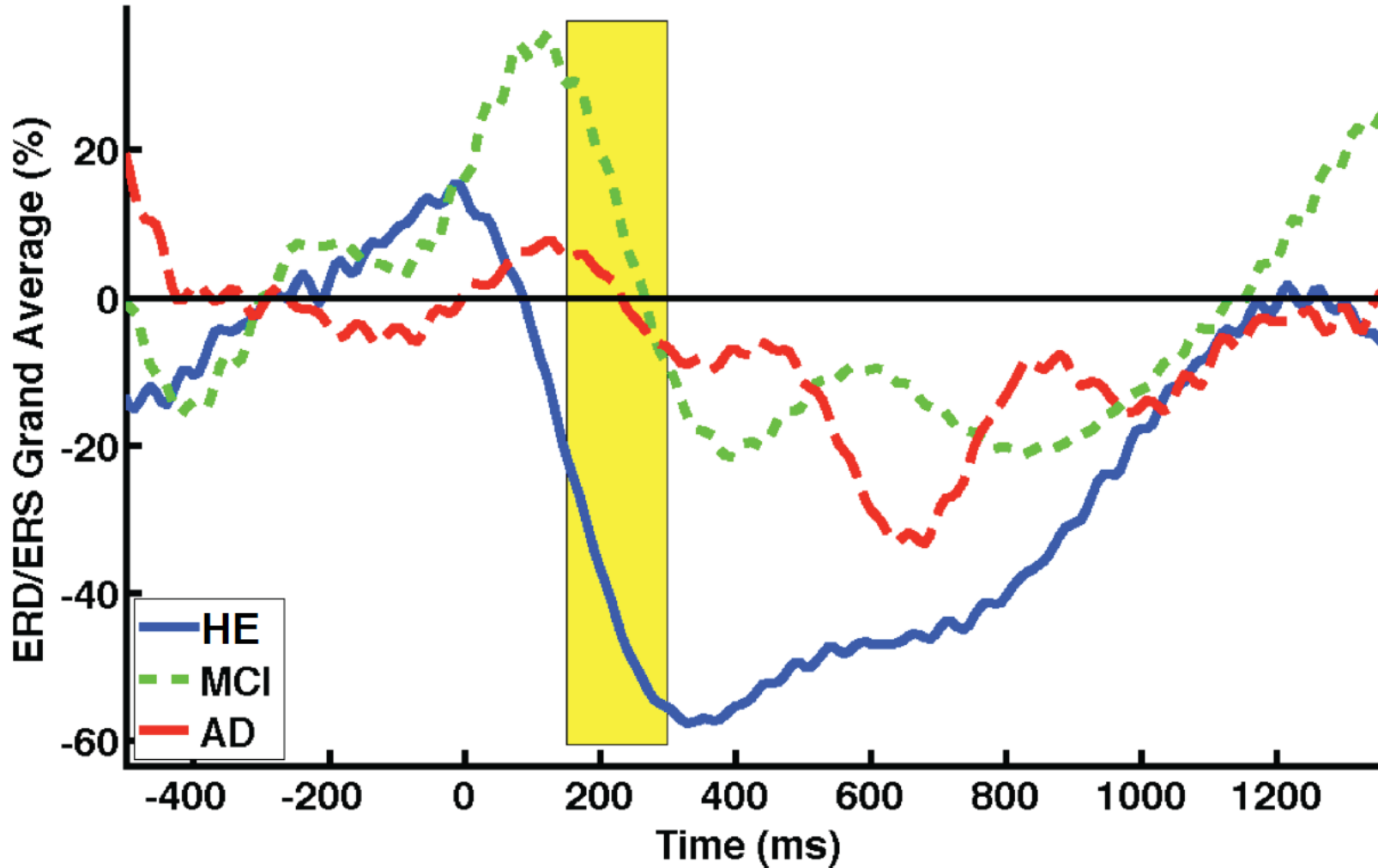
ERP results



P450: working memory update

Grand average ERP at **electrode P4** for the 1-back non-match task. Significant ERD % differences are highlighted in yellow (**HE vs. AD and HE vs. MCI**)

ERS/ERD results



Grand average ERD on alpha band at TP7 (2-back match task, HE vs. MCI)

Novel task-oriented AD-EEG technique (yet unpublished)

A new method for diagnosis support of mild cognitive impairment through EEG rhythms source location during working memory tasks

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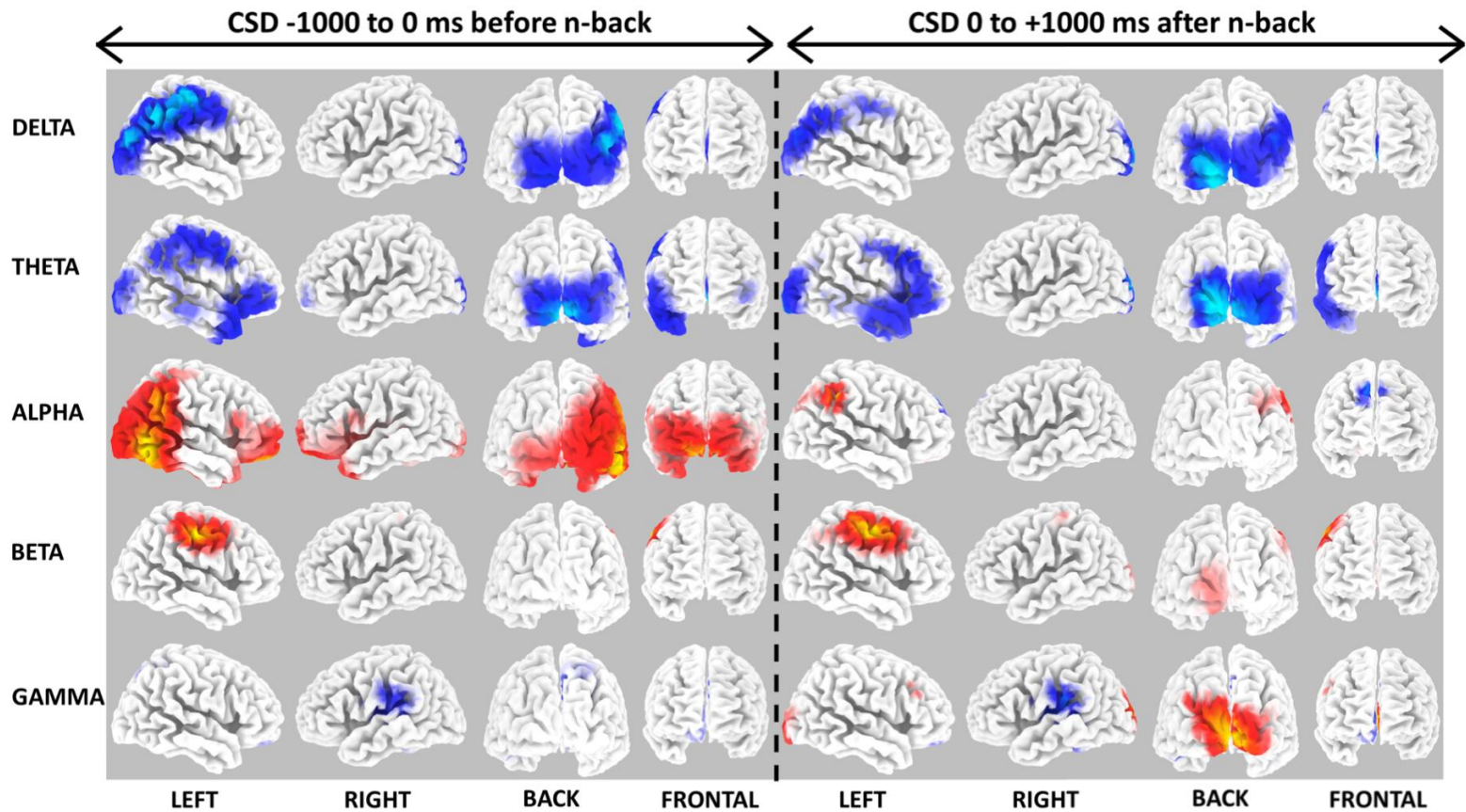
Novel task-oriented AD-EEG technique (yet unpublished)

- Traditional technique for task-oriented EEG:
 - Use of classic ERP and/or ERS/ERD
 - Focus only on post-stimulus period
- Novel technique for task-oriented EEG:
 - Use of **LORETA resting-state analysis**
 - Focus on **both pre- and post-stimulus periods**

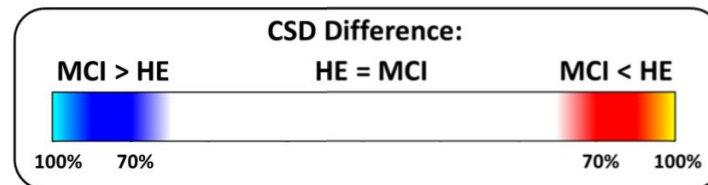
Novel task-oriented AD-EEG technique (yet unpublished)

Working Memory Epochs (WME)

Event-Related Epochs (ERE)



CSD: Current Source Density



Novel task-oriented AD-EEG technique (yet unpublished)

Group	HE	MCI	p-value
No. Participants	22	19	
No. Female	12	9	
Age	78.98±4.3	80.17±5.6	0.4442
Education	14.2±4.1	14.16±4.1	0.9852

- **Feature extraction for machine learning prediction (SVM classifier)**
- **The CSD of Brodmann regions containing the top 30% most different voxels (HE x MCI) for each band and condition (WME and ERE) formed the features**
- **WME contained 80 features and ERE contained 42 features**
- **25% of participants were separated just for feature selection**
- **31-fold cross-validation results on the remaining 75% of participants**

Feature Set	Accuracy	<i>F1</i> score	Specificity	Sensitivity
WME	0.84 ± 0.02	0.82 ± 0.03	0.86 ± 0.02	0.82 ± 0.04
ERE	0.84 ± 0.02	0.82 ± 0.03	0.89 ± 0.03	0.79 ± 0.04
WME + ERE	0.94 ± 0.02	0.93 ± 0.02	0.94 ± 0.02	0.94 ± 0.03

Thanks!



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- ✓ 2011/21385-2 (BPE)
 - ✓ 2012/14793-0 (Publications)
 - ✓ 2015/09510-7 (Regular)
 - ✓ 2017/15243-7 (Regular)
 - ✓ 2018/03655-1(BPE)
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