

Introduction

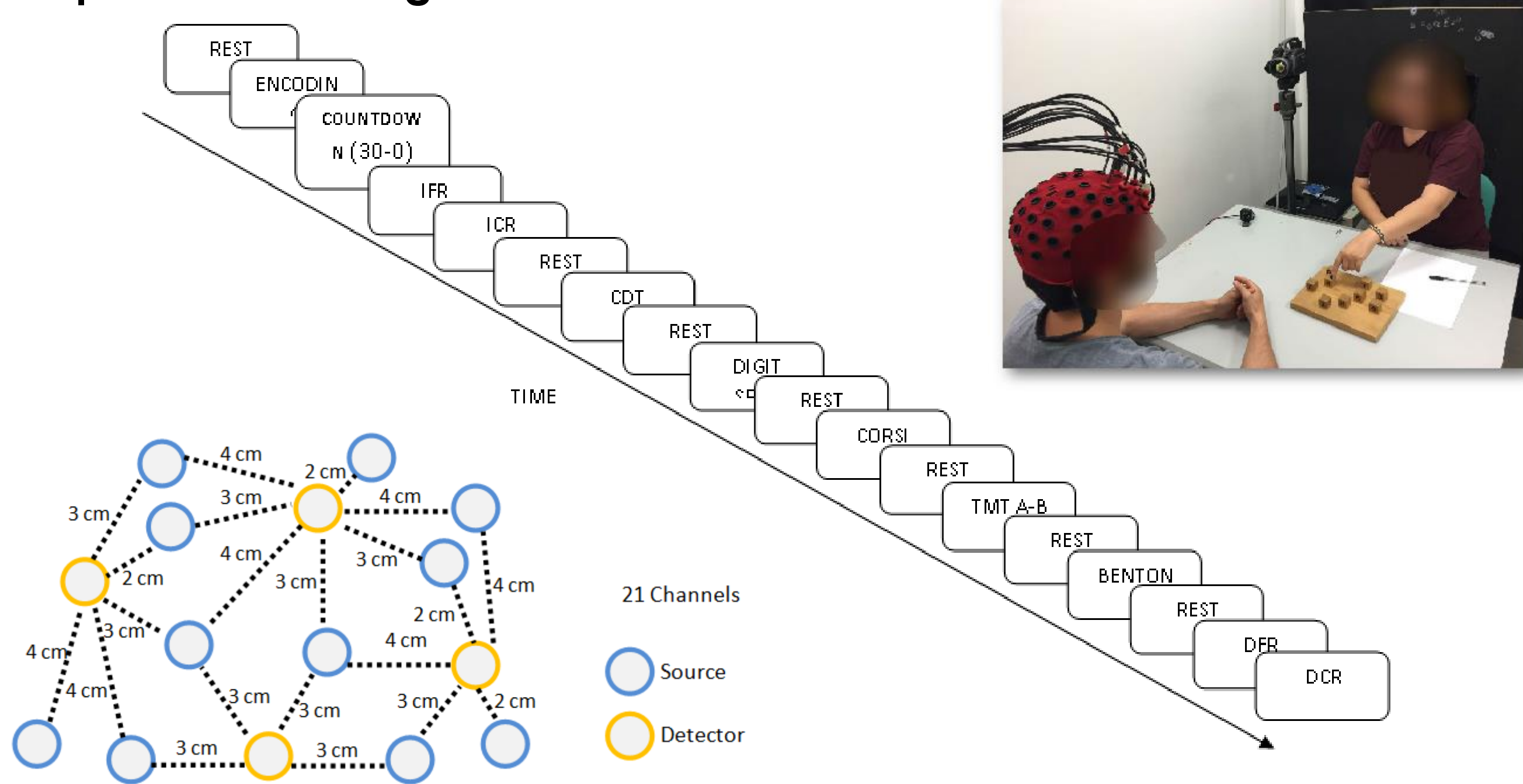
Free and Cued Selective Reminding Test¹ (FCSRT) is a validated test to define memory impairment for early diagnosis of Alzheimer's Disease (AD). Aim of the present study is to search for evidence of fNIRS signal the impairment assessed by FCSRT by the acquisition of the functional Near InfraRed Spectroscopy (fNIRS) signal during the administration of the FCSRT. Given the ecological conditions of this test, it's impossible to create a proper design matrix, so we proposed to investigate the complexity of fNIRS signal during specific phases of the FCSRT, that is Immediate Free Recall (IFR) and Delayed Free Recall (DFR), that are more indicative of AD. In particular, it was used the Sample Entropy² algorithm and a Multi Scale approach to discriminate healthy people from the patients. According to Villancourt and Newell³ ageing or disease increases the output complexity of a physiological system by presenting a dysregulation of neurobiological patterns in neural response. Therefore we supposed that AD brain signals should present higher value of entropy than controls. To the best of our knowledge, this it's the first time that such analysis of complexity is carried on fNIRS signal measured during a working memory test in completely ecological conditions.

Materials and Methods

Participants:

- N. 11 patients early AD (mean age: 72.2 ± 4.5 years)
- N. 11 healthy controls (mean age: 67.5 ± 5.0 years)

Experimental Design:



Frequency-domain oximeter (Imagent, ISS Inc.):

- Modulation Frequency: 110 MHz.
- Light Sources: 32 laser diodes emitting at 690 nm and 830 nm.
- Detectors: 4 PMTs Sensors.
- Home-made pad placed over PFC centered over Fp in the 10-20 EEG system

Data Analysis

Registration of the onset of the different part of the test by the video

Preprocessing with Homer2:

1. Intensity to OD
2. OD to Concentration
3. PCAFilter
4. Bandpass Filter ($h_p=0.01$ Hz; $l_p=0.4$ Hz)
5. Remove MotionArtifact
6. Cbsi

Wilcoxon-Mann-Whitney test and ROC curves

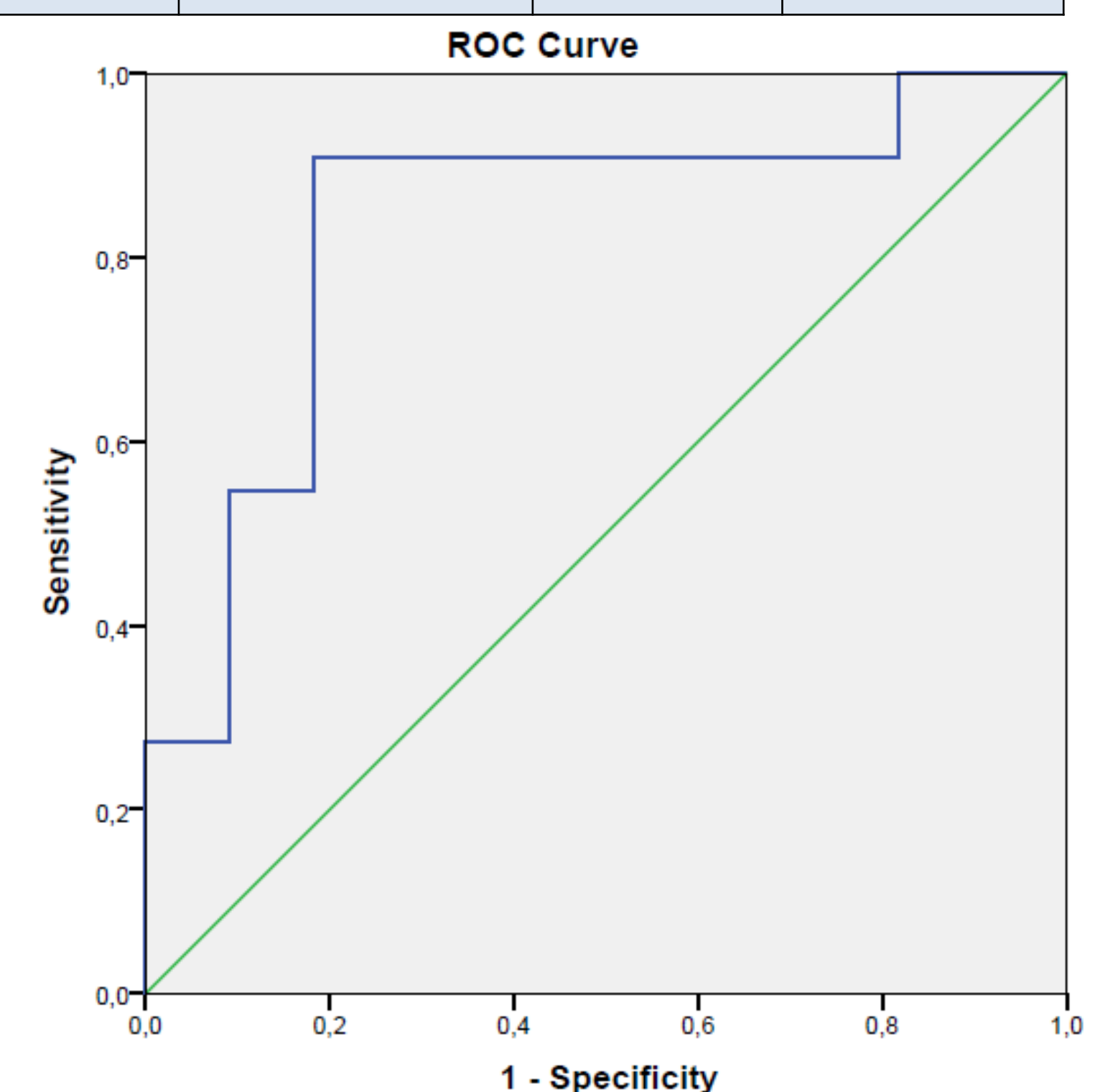
SE and MSE for Oxy and Dxy data

The parameters chosen for the calculation of SE and MSE are:

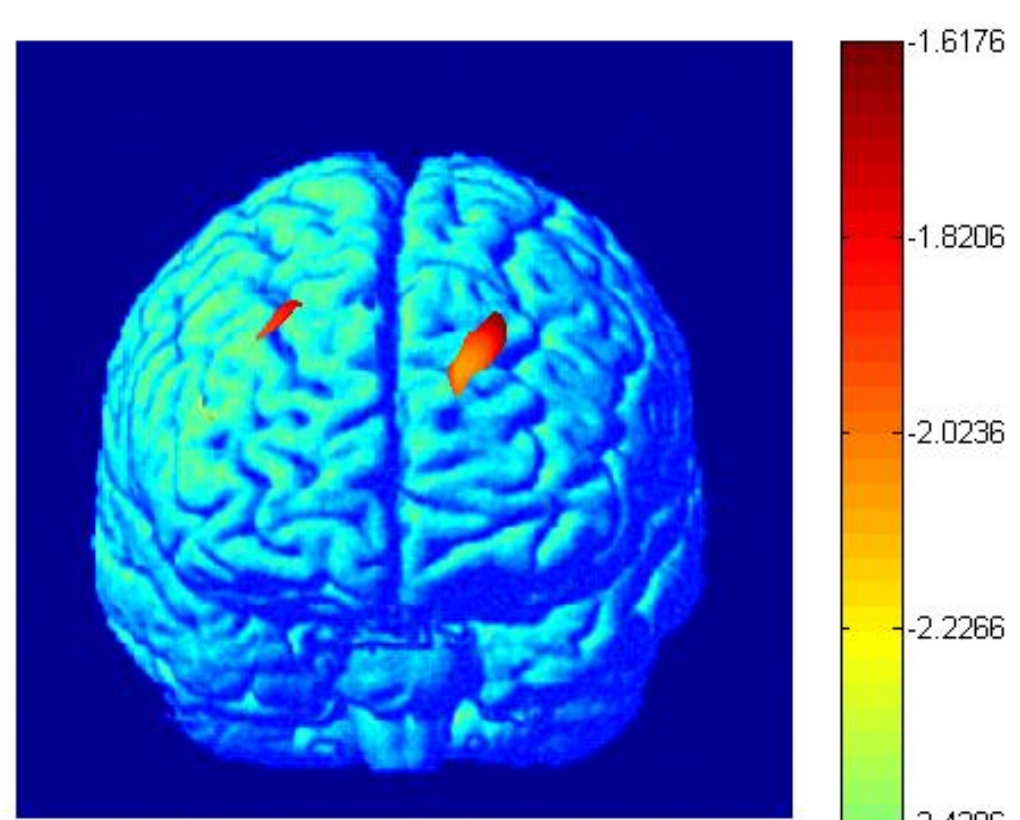
- $m=2$;
- $r=0,2 \cdot SD$;
- $\tau=[2;3]$;

Results and Discussion

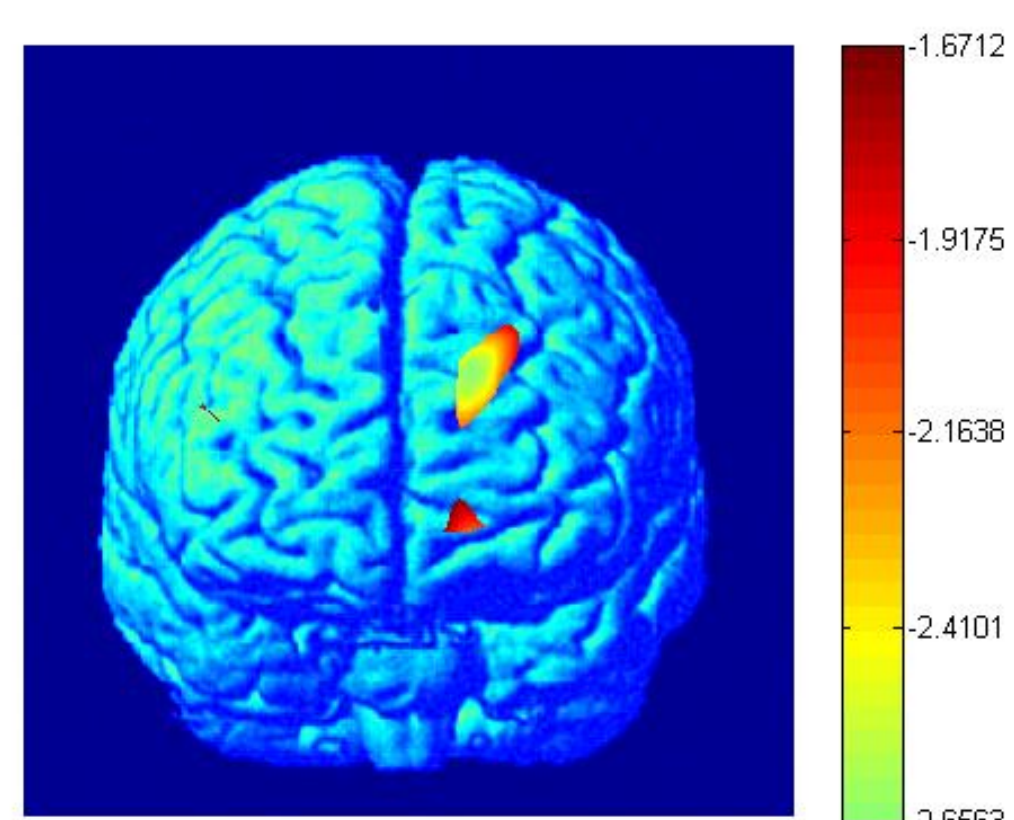
Area	Std.Error (Under the nonparametric assumption)	Asymptotic Sig. (null hypothesis: true area=0.5)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.835	0.094	0.008	0.651	1.000



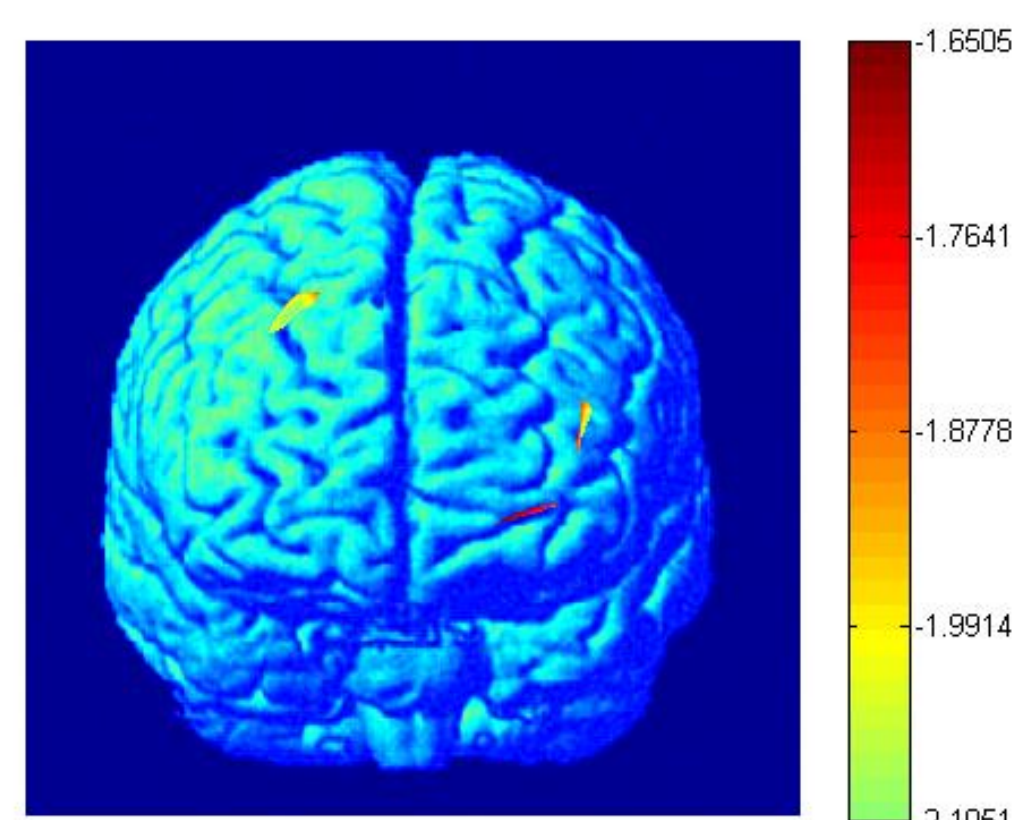
DFR, Sample Entropy oxyhemoglobin



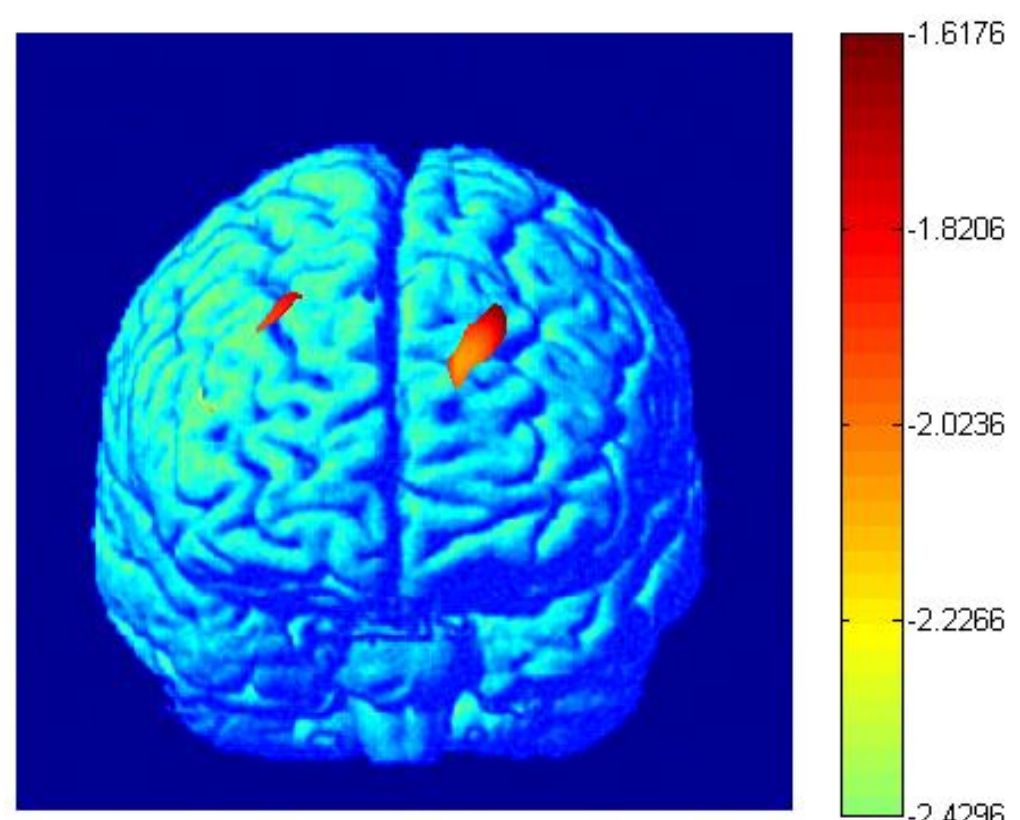
DFR, MSE ($\tau=2$) oxyhemoglobin



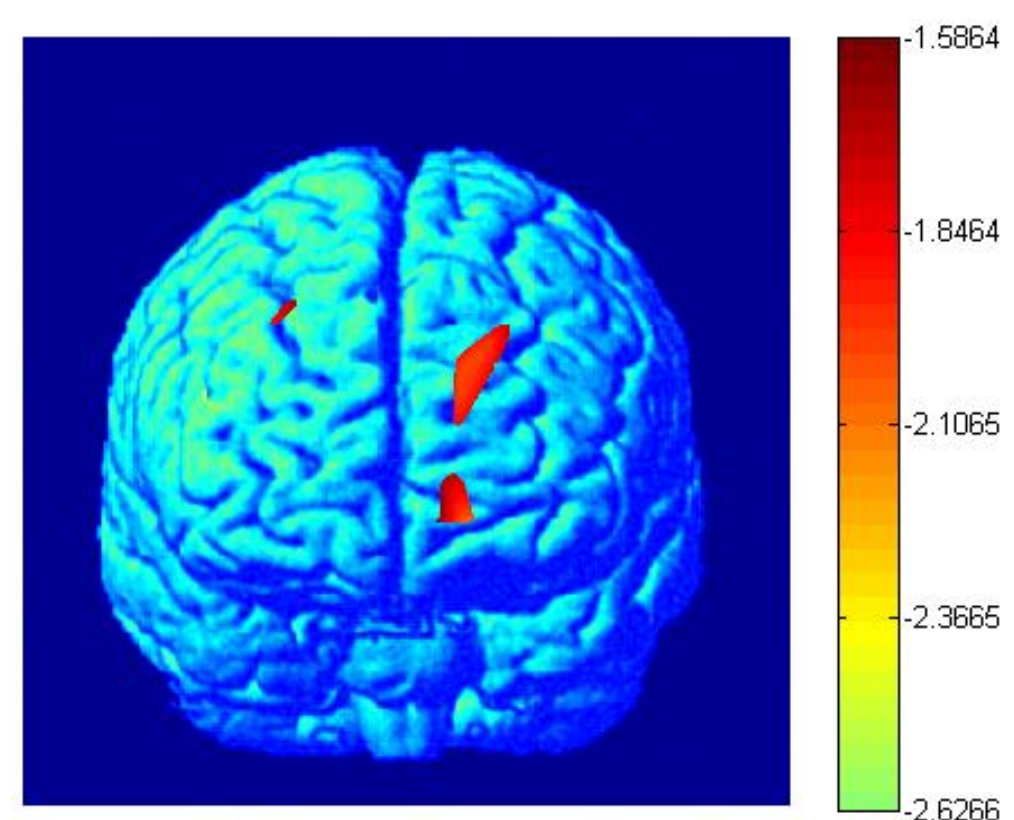
IFR, Sample Entropy oxyhemoglobin



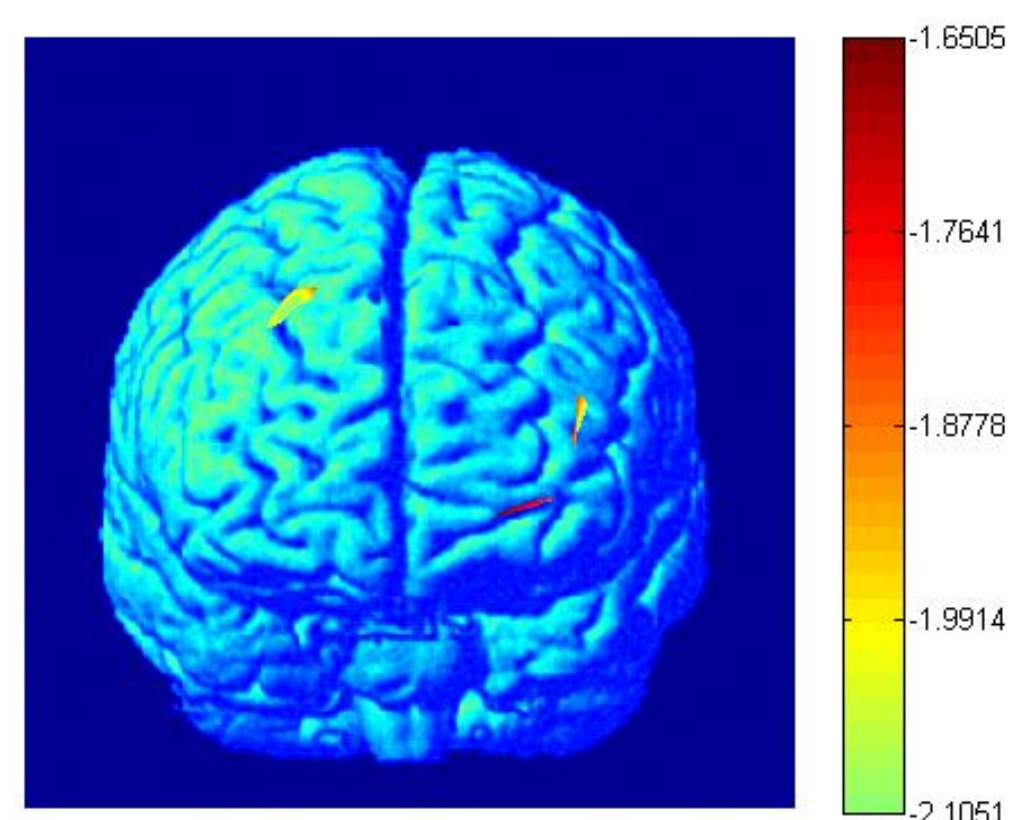
DFR, Sample Entropy deoxyhemoglobin



DFR, MSE ($\tau=2$) deoxyhemoglobin



IFR, Sample Entropy deoxyhemoglobin



Wilcoxon Test z-values HC vs AD

CONCLUSIONS

- The temporal scales more appropriate to investigate the complexity of the neurovascular coupling are $\tau=1$ and $\tau=2$;
- As we supposed, differences between the two groups are found during IFR and DFR, with patients presenting higher values of Entropy
- Largest statistically significant difference are found for channels covering Brodmann area 9 and 46.

FUTURE WORKS

- To test different definitions of Entropy
- To enlarge the number of subjects

[1] Lemos, Raquel, et al. "The free and cued selective reminding test: Validation for mild cognitive impairment and Alzheimer's disease." *Journal of neuropsychology* 9.2 (2015): 242-257.
 [2] Moorman, Physiological time-series analysis using approximate entropy and sample entropy (2000). *Am. J. Physiol. Heart Circ. Physiol.* 278, H2039-H2049.
 [3] Vaillancourt, David E., and Karl M. Newell. "Changing complexity in human behavior and physiology through aging and disease." *Neurobiology of aging* 23.1 (2002): 1-11.