URSI'19

XXXIV SIMPOSIUM NACIONAL DE LA UNIÓN CIENTÍFICA INTERNACIONAL DE RADIO

SEVILLA, 4 al 6 de septiembre de 2019

LIBRO DE RESÚMENES

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ORGANIZAN

UNIVERSIDAD DE SEVILLA

Escuela Técnica Superior de INGENIERÍA DE SEVILLA

PATROCINAN

KEYSIGHT TECHNOLOGIES

ROHDE&SCHWARZ

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Miércoles, 04/09/2019					
8:00 - 9:30	**Acreditación** *Acceso puerta 1 edificio ETSI*				
9:30 - 11:00	**Sesión 1.1**: Telemática *Aula 002*	**Sesión 1.2**: Sesión especial - Avances en el procesado de señales cerebrales *Aula 003*	**Sesión 1.3**: Sesión especial - Comunicaciones por Satélite (I) *Aula 005*	**Sesión 1.4**: Aplicaciones Biomédicas *Aula 006*	**Sesión 1.5**: Metamateriales *Aula 007*
11:00 - 11:30	**Pausa para Café** *Patio central planta baja edificio ETSI*				
11:30 - 11:50	**Acto de Apertura del Congreso URSI 2019** *Salón de Actos*				
11:50 - 12:40	**Conferencia Plenaria (Profª. Almudena Suárez)** *Salón de Actos*				
12:45 - 14:00	**Sesión 2.1**: Radiación, Dispersión y Radiopropagación (I) *Aula 002*	**Sesión 2.2**: Comunicaciones Móviles e Inalámbricas (I) *Aula 003*	**Sesión 2.3**: Sesión especial - Avances en modelado y simulación de circuitos no-lineales *Aula 005*	**Sesión 2.4**: Sesión especial - Electromagnetismo Computacional (I) *Aula 006*	**Sesión 2.5**: Sesión especial - Técnicas y tecnologías de fabricación para antenas y dispositivos de RF (I) *Aula 007*
14:00 - 15:30	**Almuerzo de Trabajo** *Patio central planta baja edificio ETSI*				
15:30 - 17:30	**Sesión 3.1**: Radiación, Dispersión y Radiopropagación (II) *Aula 002*	**Sesión 3.2**: Comunicaciones Móviles e Inalámbricas (II) *Aula 003*	**Sesión 3.3**: Sesión especial - Comunicaciones por Satélite (II) y Mesa Redonda *Aula 005*	**Sesión 3.4**: Sesión especial - Electromagnetismo Computacional (II) *Aula 006*	**Sesión 3.5**: Sesión especial - Técnicas y tecnologías de fabricación para antenas y dispositivos de RF (II) *Aula 007*

SESIÓN 1 Miércoles, 04/09/2019 09:30 - 11:00

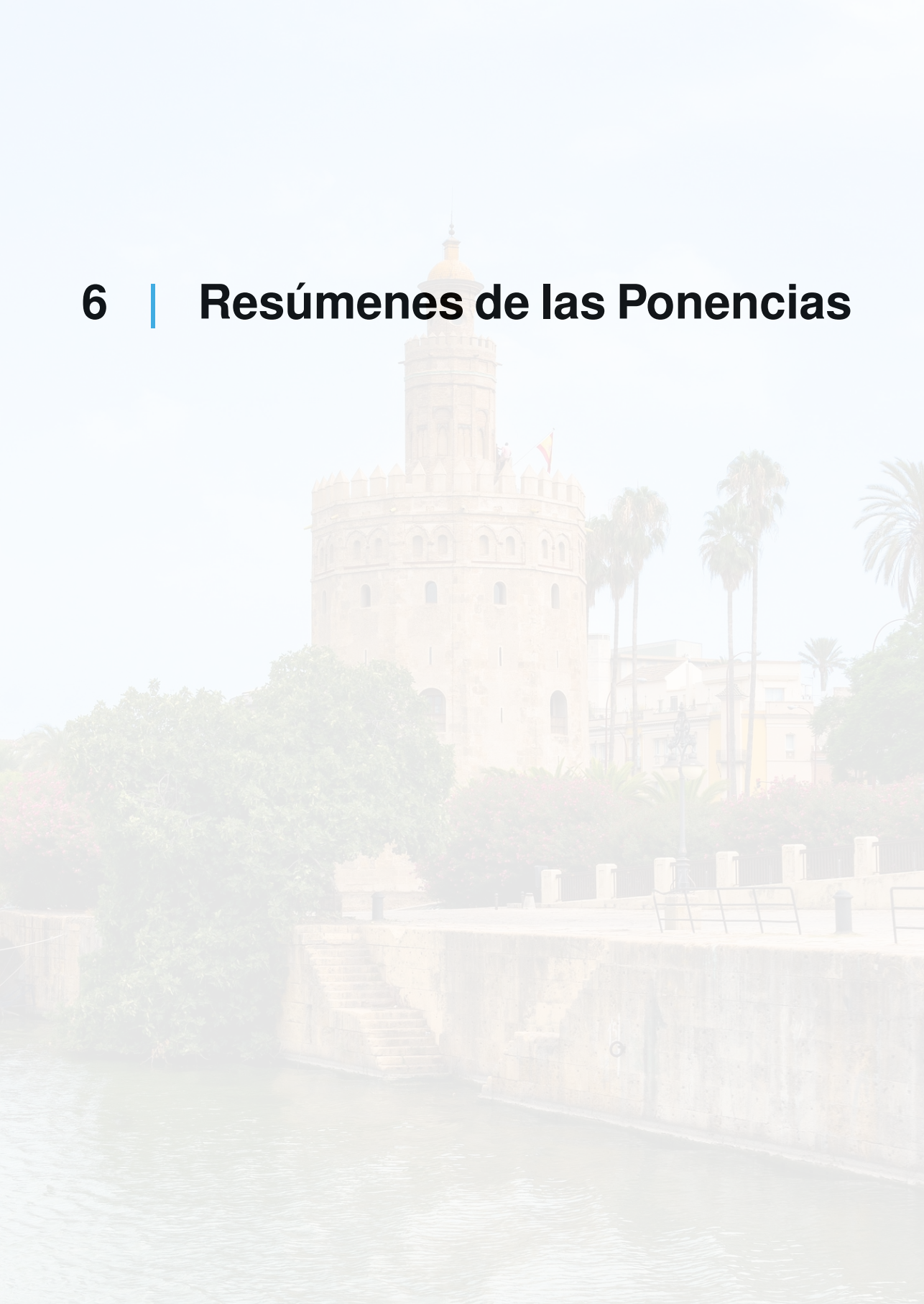
Sesión 1.1 Telemática

Lugar: **Aula 002**
Presidenta de la sesión: **Isabel Román Martinez** (Universidad de Sevilla)
Presidente de la sesión: **Antonio J. Sierra Collado** (Universidad de Sevilla)

Sesión 1.2 Sesión especial - Avances en el procesado de señales cerebrales

Lugar: **Aula 003**
Presidente de la sesión: **Sergio Cruces** (Universidad de Sevilla)
Presidente de la sesión: **Rubén Martín Clemente** (Universidad de Sevilla)

6 | Resúmenes de las Ponencias



Sesión 1.2

Sesión especial - Avances en el procesado de señales cerebrales

Miércoles, 04/09/2019
Hora: **09:30 - 11:00**. Lugar: **Aula 003**

09:30 - 09:50 Assessing the influence of cognitive reserve in EEG signals through Alzheimer's Disease progression

Rodríguez, Víctor [(1)]; Poza, Jesús [(1)]; Gómez, Carlos [(1)]; Tola-Arribas, Miguel Ángel [(2)]; Cano, Mónica [(2)]; Hornero, Roberto[(1)]
[(1)] *Grupo de Ingeniería Biomédica, Universidad de Valladolid, España;* [(2)] *Hospital Universitario Río Hortega, Valladolid, España*

Alzheimer's Disease (AD) has a high economical, social, and clinical impact in our society, especially in most developed world. It has been proven that its progression is influenced by many factors such as age, gender, genetics of cognitive reserve (CR). In the case of the latter, its influence in neural signals during AD progression has been scarcely studied. To understand how CR influences brain activity, electroencephalographic (EEG) recordings were analysed as a function of the CR by using spectral and nonlinear methods. The database was composed by 160 subjects divided in 3 groups (controls, mild cognitive impairment subjects, and AD patients) and 2 CR levels (low and high). Results showed that the spectral and nonlinear EEG parameters are influenced by CR. Also, it has been observed using cognition, memory, and functional disability tests that a high CR provides more resilience against AD progression, but also a faster decline in the later AD stages. We conclude that CR has a remarkable influence in AD progression, which can be observed by analysing neurophysiological signals.

7 | Índice de Autores

Assessing the influence of cognitive reserve in EEG signals through Alzheimer's Disease progression

Víctor Rodríguez-González(1), Jesús Poza(1), Carlos Gómez(1),
Miguel Ángel Tola-Arribas(2), Mónica Cano(2), Roberto Hornero(1).
victor.rodriguez@gib.tel.uva.es, jesus.poza@tel.uva.es, carlos.gomez@tel.uva.es
mtoar@saludcastillayleon.es, mcanopo@saludcastillayleon.es, robhor@tel.uva.es.
(1)Grupo de Ingeniería Biomédica. Universidad de Valladolid. Paseo de Belén, 15. 47011 Valladolid.
(2)Hospital Clínico Universitario Rio Hortega. Av. Ramón y Cajal, 3, 47003 Valladolid.

***Abstract*—Alzheimer's Disease (AD) has a high economical, social, and clinical impact in our society, especially in most developed world. It has been proven that its progression is influenced by many factors such as age, gender, genetics or cognitive reserve (CR). In the case of the latter, its influence in neural signals during AD progression has been scarcely studied. To understand how CR influences brain activity, electroencephalographic (EEG) recordings were analysed as a function of the CR by using spectral and nonlinear methods. The database was composed by 160 subjects divided in 3 groups (controls, mild cognitive impairment subjects, and AD patients) and 2 CR levels (low and high). Results showed that the spectral and nonlinear EEG parameters are influenced by CR. Also, it has been observed using cognition, memory, and functional disability tests that a high CR provides more resilience against AD progression, but also a faster decline in the later AD stages. We conclude that CR has a remarkable influence in AD progression, which can be observed by analysing neurophysiological signals.**

I. Introduction

Dementia due to Azheimer's Disease (AD) is a neurodegenerative disease that alters neural activity, with cognitive, conductual, and functional abnormalities [1]. Mild cognitive impairment (MCI) is an early stage of dementia where the patient exhibits a cognitive impairment away from normal ageing, but not enough to be diagnosed as dementia [1]. Both diseases are characterised by the emergence of amyloid-beta and tau proteins [2]. Sometimes MCI is considered as a prodromal state of AD [1]. In most developed countries, AD is the most common dementia with an increasing economical, social and clinical impact [3]. It is thought that about 47 million people were suffering from AD in 2015, and for 2020 this number could increase up to 132 millions [3]. AD affects, in Spain alone, about a million people with an economical cost around 22000 M € [4].

The progression of dementia due to AD can be influenced by many factors, such as age, sex, and genetics [5]. In this regard, ageing is considered the most important risk factor to develop AD, with a dramatically increasing number of AD incidence with age [5]. Sex also influences AD progression; several studies suggest a higher AD risk in females [5]. In addition, genetics play an important role in the genetic variants of AD, with APOE-η4 allele carriers showing a high correlation with an increasing AD impact [5]. Accumulating evidence supports the influence of these factors on brain activity [5]–[7].

Cognitive reserve (CR) refers to the differences between individuals in cognitive and functional processes that the brain performs to cope with the disruptions of AD [8]. A high cognitive reserve is related with the participation in cognitive stimulating experiences (like education, leisure activity or occupational attainments) [9]. Recent evidence supports the hypothesis that AD progression is strongly influenced by CR, providing subjects with higher CR more resilience against pathological processes that accompanied the disease, but with a faster decline at advanced AD stages [8]. Nevertheless, cognitive reserve has been barely studied. A few studies addressed its influence on brain metabolism using positron emission tomography (PET) [10], [11] or on brain connectivity using functional magnetic resonance imaging (fMRI) [12]. However, to the best of our knowledge, its impact in electrophysiological brain signals has not been previously explored.

Electrophysiological brain recordings contain information about electric and magnetic properties of signals generated by neurons [2]. The most widely used techniques to measure neuronal activity are electroencephalography (EEG) and magnetoencephalography (MEG) [2]. Both of them provide a high temporal resolution with low invasivity [2]. Nevertheless, while MEG has an improved spatial resolution, EEG offers low economical cost and thus it is widely used in clinical settings [2]. EEG records electrophysiological signals from neurons at scalp level [2]. This provides information about brain functioning in real-time, which allows to analyse the transmission and processing of neural information [2].

We hypothesised that cognitive reserve could influence EEG signals, as other factors do. In order to assess this issue, EEG signals were analysed using two complementary methodologies: spectral and nonlinear analyses. Hence, the aim of this study was to obtain a deeper understanding of the influence of CR in neural activity during AD progression by analysing the evolution of different EEG-based parameters.

II. Materials and methods

A. Subjects

The study database was composed by 37 cognitively healthy elderly controls (HC), 51 patients with MCI due to AD, and 72 patients with dementia due to AD. MCI and AD patients were diagnosed according to the criteria of the National Institute on Ageing and Alzheimer's Association (NIA-AA), while HC were volunteers with no symptoms of neurological disorders nor pathological background [13]. Table I shows

TABLE I
SOCIO-DEMOGRAPHIC AND CLINICAL INFORMATION OF THE DATABASE USED IN THIS STUDY

Data[a]	**Group**		
	Controls	MCI	AD
Number of subjects	37	51	72
Age (years)	76.3±3.8	75.8±6.4	80.1±5.5
Gender (male:female)	12:25	20:31	29:43
Education level (A:B:C)[b]	1:10:26	6:29:16	23:30:19
MMSE[c]	28.8±1.1	26.9±1.8	20.7±3.9
M@T[d]	45.1±4.3	31.6±5.6	20.14±6.46
Bayer-ADL[e]	1.19±0.20	2.94±0.97	5.89±1.55
CRIq[f]	10.68±4.37	7.49±3.92	7.03±4.85

[a]Values are given as: mean ± standard deviation. [b]A: below primary education; B: primary education; C: secondary education or above. [c]MMSE: Mini-Mental State Examination (range: [0 30]). [d]M@T: Memory Alteration Test (range: [0 50]). [e]Bayer-ADL: Bayer Activities Daily Living (range: [0 10]). [f]CRIq: Cognitive Reserve Index questionnaire (range: [0 25]).

socio-demographic and clinical data of the population. Mini-Mental State Examination test (MMSE) was used to evaluate cognition. To assess functional disability, Bayer Activities of Daily Living scale (Bayer-ADL) was used. The verbal episodic and semantic memory was evaluated with the Memory Alteration Test (M@T) [14]. The Spanish version of the Cognitive Reserve Index questionnaire (CRIq) was used to measure the cognitive reserve [15]. Patients were divided into two groups according to their results in CRIq: low CR (ranged from 0 to 9), and high CR (ranged from 10 to 25). The groups with low CR were composed by 16, 39, and 56 subjects for HC, MCI and AD patients respectively. Additionally, the HC, MCI, and AD patients groups with high CR were composed by 21, 12, and 16 subjects respectively.

Patients and caregivers were informed of the purpose and experimental protocol of the research. All of them gave informed consent to be enrolled in the study. The Ethical Committee of the 'Hospital Universitario Río Hortega' (HURH, Valladolid, Spain) endorsed the protocol, which was designed in accordance with the considerations of the Declaration of Helsinki (World Medical Association).

B. EEG Recordings

EEG signals were recorded with a EEG system (XLTEK®, Natus Medical) with 19 channels, located at the Department of Clinical Neurophysiology of the HURH. The electrodes were placed in the positions Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, P3, P4, O1, and O2 according to the International 10-20 system. The sampling frequency used was 200 Hz. During EEG acquisition, subjects were asked to remain awake with closed eyes. To avoid drowsiness, subjects were continuously monitored during EEG recording.

According to the protocol, 5 minutes of resting-state activity were recorded for each subject. The following preprocessing pipeline was applied [16]: (i) notch filter at 50 Hz to remove line noise, (ii) bandpass filter in the band of interest (1-70 Hz) to reduce noise bandwidth, (iii) Independent Component Analysis (ICA) to remove noisy components from the signals, and (iv) selection of 5 second artifact-free epochs by visual inspection.

C. Spectral and nonlinear parameters

Spectral and nonlinear parameters were used to characterise the neural activity extracted from the EEG recordings [16]. Median Frequency (*MF*) was used to quantify the spectral content of the signals, while its complexity was measured using Lempel-Ziv Complexity (*LZC*).

1) Median Frequency: MF is the frequency that divides the power of the spectrum in two halves of equal power [17]. It summarizes in one measure the distribution of the spectral content of the Power Spectral Density (*PSD*). Thereby, it is useful to quantify the 'slowing' or 'acceleration' of oscillatory neuronal activity [17].

To calculate *MF*, *PSD* has to be firstly estimated. The *PSD* was calculated for each epoch using the Blackman-Tukey method, which is the Fourier Transform of the autocorrelation function [17]. The *PSD* was calculated with 5-second non-overlapping windows [16]. From this function, *MF* can be calculated as follows:

$$\sum_{1Hz}^{MF} PSD(f) = 0.5 \sum_{1Hz}^{70Hz} PSD(f). \tag{1}$$

Afterwards, the *MF* values from all epochs and channels were averaged, thus obtaining the grand-averaged *MF* for each subject.

2) Lempel-Ziv Complexity: LZC is a measure of complexity in Kolmogorov's sense, assigning larger values to more complex signals [18].

It is based on a coarse-grain analysis of the data, so the signal has to be firstly converted into a binary sequence comparing each sample with a threshold T_d [18]. The threshold was set as the median amplitude of the signal in each channel due to the robustness of the median to outliers [19].

$$s_d(i) = \begin{cases} 0 & if \quad x_d(i) < T_d \\ 1 & if \quad x_d(i) \geq T_d \end{cases}, \tag{2}$$

where $x_d(i)$ is the signal in sensor *d*, and $s_d(i)$ is the converted signal of sensor *d*. After the conversion, the signal s_d was scanned and the number of times a new subsequence of characters appears was counted in $c(n)$. Finally, $c(n)$ was normalised to restrict the *LZC* value between 0 and 1, as recommended by previous studies [19]:

$$LZC = \frac{c(n)}{N/log_2(N)}, \tag{3}$$

where N is the length of the signal. As with *MF*, *LZC* values from all channels and epochs were averaged. More details about the calculation of the *LZC* can be found in [18].

D. Statistical analysis

In a first step, an exploratory analysis was conducted to assess the distribution of *MF* and *LZC* values. Neither the data nor their log-transformed values met the parametric assumptions of normality (Lilliefors) or homoscedasticity (Chi-square variation test). Thereafter, nonparametric tests were applied to assess statistical differences.

Differences between pathological groups (within CR groups) were assessed using Kruskal-Wallis test. To evaluate whether exist differences between CR groups (within pathological groups), Mann-Whitney *U* tests were used.

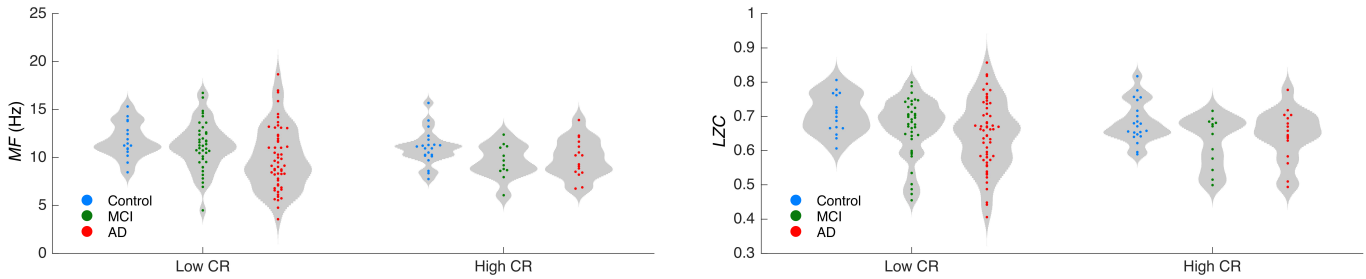


Fig. 1. Distribution of (a) *MF* and (b) *LZC* for HC, subjects with MCI due to AD, and patients with dementia due to AD. Subjects have been divided in two groups according to their cognitive reserve: low CR (from 0 to 9), and high CR (from 10 to 25)

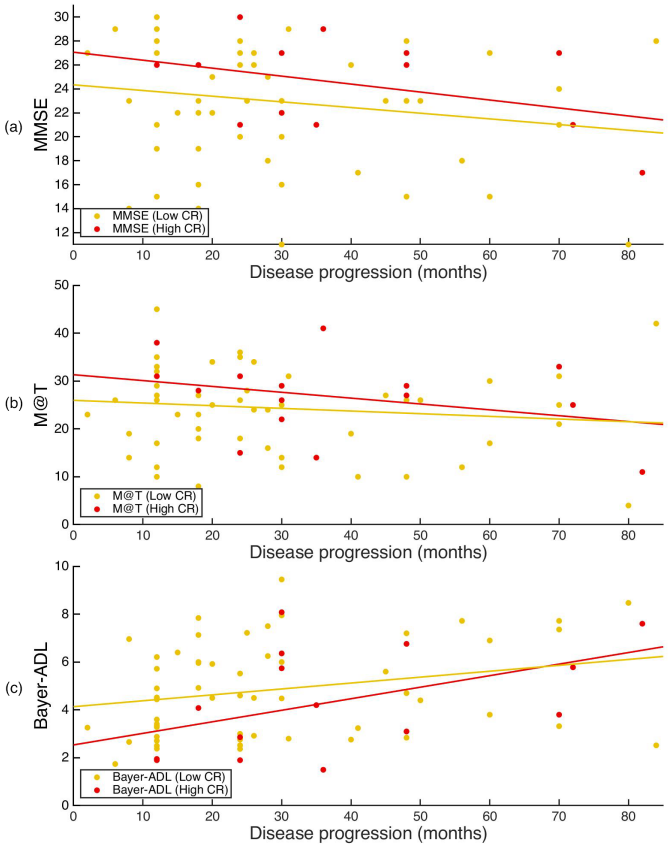


Fig. 2. Scoring of (a) cognitive (MMSE), (b) memory (M@T), and (c) function (Bayer-ADL) tests for MCI and AD patients with low CR and high CR as a function of disease progression.

All signal processing and statistical analyses were performed using MATLAB® version 2018a (Mathworks, Natick, MA).

III. Results

A. Spectral and nonlinear parameters

Fig. 1 shows the evolution of *MF* and *LZC* with the progression of dementia due to AD for both CR groups. For the subjects with low CR, *MF* decreases as AD progresses. However, subjects with high CR display similar *MF* values for all groups (HC, MCI and AD). Statistically significant differences (p-value = 0.038, Mann-Whitney test) were observed for *MF* only in the MCI group. Furthermore, *LZC* values for the group with low CR, shows a decrease with AD progression. However, in the group with high CR, *LZC* values for AD and MCI patients are alike, with slightly higher values for HC. Both, *MF* and *LZC* showed statistically significant differences among HC, MCI, and AD for low CR (p-value = 0.011 and 0.044 respectively, Kruskal-Wallis test).

B. Evolution of cognitive tests

The evolution of different cognitive tests (Bayer-ADL MMSE and T@M) as a function of the disease progression were depicted in Fig. 2. To obtain the disease progression parameter, each patient and their caregivers were asked about how long they have suffered from dementia symptoms. According to the results, cognition (MMSE), memory (M@T), and functional disability (Bayer-ADL) decrease as the disease progresses following a similar trend: higher CR implies better performance in tests, but faster decline.

IV. Discussion

A. Spectral and nonlinear parameters

Slowing and loss of complexity are two of the most well-known effects of AD in neural signals [20]. *MF* summarises the slowing of neural activity [17], whereas *LZC* reflects the loss of complexity [19]. In Fig. 1 it can be observed that these effects are more noticeable in subjects with low CR. Despite *MF* and *LZC* are not measuring the same properties, they are strongly related [20]. The underlying causes of these effects are not clear, but neuronal death, senile plaques, or neurotransmitter deficiency could be the mechanisms, among others, responsible of slowing and loss of complexity in brain signals [21].

B. Evolution of cognitive tests

Cognitive reserve has been previously proven to influence the progression of dementia due to AD [8]. Stern hypothesised that individuals with high level of CR should show higher resilience to the pathology, however they also should suffer from a faster decline after AD clinical presentation [8]. This hypothesis is summarised in Fig. 3, where the evolution of AD pathology as a function of CR is depicted. With the latter in mind, patients with higher CR would have a more severe pathological state when AD is diagnosed [8].

Our results are in line with the previous hypothesis, as cognition, memory, and functional disability showed higher values with a sharper decline for subjects with high CR. This may suggest that subjects in Fig. 2 are in the second part of Fig. 3. AD diagnosis is usually made in a late stage, which may explain that the first part of Fig. 3 is not reflected in the evolution of cognition, memory, and functional disability test scores in Fig. 2 [22].

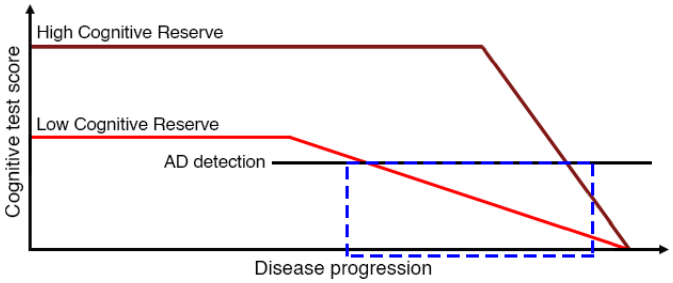


Fig. 3. Evolution of AD pathology as a function of cognitive reserve. Adapted from [8]. The blue square shows, approximately, the range where the subjects of our database fall within.

C. Limitations and future lines

There exist some considerations in the study that have to be mentioned. First of all, the sample size should be increased in order to pair all the groups, and to increase the statistical power of the tests. Secondly, longitudinal recordings would be of great interest to assess the influence of CR for each subject. Likewise, future studies should address the analysis of other parameters to increase the understanding on how the CR influences EEG signals. Furthermore, disease progression was calculated by asking patients and caregivers how long they have suffered from AD symptoms. This could bias our data and so, it should be taken into account in futures studies. Finally, all the patterns have been studied at scalp-level, but it would be also interesting to assess them at source-level.

V. Conclusions

Our findings showed an influence of CR in three cognitive domains (cognition, memory, and functional disability) measured using different cognitive tests, which is in line with previous studies where a remarkable influence of CR in AD progression was observed. Furthermore, it was found that EEG-based analyses can be biased by CR. Future research is needed, but our findings suggest that the CR is a confounding factor that should be accounted when analysing neural signals.

Acknowledgements

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