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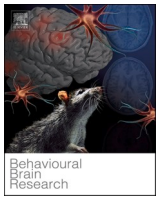

Research article

Individual posterior alpha rhythms and cognitive reserve as possible early prognostic markers in people with subjective memory complaints

Vanesa Perez [a,b], Vanesa Hidalgo [a,c,*], Alicia Salvador [a,d]

[a] Laboratory of Social Cognitive Neuroscience, IDOCAL, Department of Psychobiology, University of Valencia, Valencia, Spain
[b] Valencian International University, Valencia, Spain
[c] Department of Psychology and Sociology, Area of Psychobiology, University of Zaragoza, Teruel, Spain
[d] Spanish National Network for Research in Mental Health CIBERSAM, 28029, Spain

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ABSTRACT

Subjective memory complaints (SMCs) are a memory disorder that often precedes mild cognitive impairment (MCI) or Alzheimer's disease (AD). Both individual alpha rhythms and cognitive reserve (CR) represent key features of SMCs and provide useful tools to characterize and predict the course of the disorder. We studied whether older people with SMCs may also present some abnormal resting state electroencephalogram (rsEEG) alpha rhythms, and whether alpha rhythms are associated with CR. To do this, eyes-closed rsEEG were recorded in 68 older people with and without SMCs. The individual alpha indexes alpha/theta transition frequency (TF) and individual alpha frequency peak (IAFp) were computed. TF and IAFp were also used to determine the alpha1, alpha2, and alpha3 power frequency. Results indicated no differences in TF or IAFp between older people with SMCs and controls. The SMCs group showed a reduction in alpha3 power in comparison with controls. Specifically, women with SMCs were characterized by a significant decrease in alpha3 power compared to control women. Furthermore, only in SMCs group, greater CR was associated with slow IAFp. In sum, these results suggest that TF and IAFp are two stable indexes that are not influenced by the presence of SMCs. However, the reduction in alpha3, as observed in women with SMCs, shows an abnormal posterior rsEEG at alpha power. Finally, the compensatory mechanisms of CR appear to interact with the neurophysiological mechanisms that underlie the regulation of alpha rhythms.

1. Introduction

Identifying people in the early stages of a neurodegenerative disorder offers the opportunity to apply possible preventive measures. Therefore, subjective memory complaints (SMCs) are important as they provide insights into neurological basis of prodromal mild cognitive impairment (MCI) or Alzheimer's disease (AD; [1]). SMCs are commonly reported as the self-experienced, persistent decline in cognitive capability compared to a previous normal cognitive status [2]. Although some studies have investigated their association with objective cognitive performance in older people, the results have been inconsistent, given that not all complainers present deficits on objective cognitive assessments [3]. This lack of association has led to examining whether people with greater cognitive reserve (CR) might have more accessible resources with which to deal with cognitive decline over time. CR is defined as an active and dynamic model of reserve in which the brain adapts to a deteriorating situation by using cognitive resources to compensate for deficits [4,5]. Furthermore, the brain reserve (BR) hypothesis, focusing on neurons, synapses, and brain size, suggests that the structural brain diversity enables curtains individuals to effectively mitigate the effects of aging [6]. Conversely, the CR perspective suggests that the enduring impact of the disease is influenced by experiences acquired throughout life, including education, leisure activities, an active lifestyle, one's occupation, and social dimensions [5]. At the brain level of analysis, CR is associated with protective and compensatory mechanisms against pathological brain aging [7].

Similarly, a neurophysiological approach could also contribute to understanding SMCs. In this regard, the analysis of resting state EEG rhythms (rsEEG) is a non-invasive technique used to investigate the electrophysiological parameters of the brain activity. The anchor point for rsEEG analysis is the alpha frequency band, which dominates the EEG power spectrum in relaxed and quiet adults with their eyes closed.

* Corresponding author at: Department of Psychology and Sociology, Area of Psychobiology, University of Zaragoza, Campus Ciudad Escolar, Teruel 44003, Spain.
E-mail address: vhidalgo@unizar.es (V. Hidalgo).

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For clinical research applications, however, frequency analysis of rsEEG must consider individual differences [8]. In this regard, two frequency landmarks are recommended for analysis: (1) theta/alpha transition frequency (TF) and (2) the individual alpha frequency peak (IAFp) [9]. The TF marks the transition frequency between the theta and alpha bands, and it represents an estimate of the frequency at which the theta and alpha spectra intersect [10], whereas the IAFp represents the maximum power density peak within the alpha range instead [9]. Inter-subject differences in IAFp are reported to exhibit characteristics of a stable marker of a neurophysiological trait [9].

Most studies have argued that using IAFp provides a more accurate estimate of alpha modulated activity [11]. When the IAFp is used for the estimation of alpha activity, three alpha bands (with a width of 2 Hz each) can be distinguished, two lower alpha bands (below the IAFp: alpha1 and alpha 2) and one higher alpha band (above the IAFp: alpha3) [9]. In addition, changes in alpha rhythms have consistently been associated with neurodegenerative diseases such as AD and MCI. For instance, Gouw et al. [12] identified an association between lower IAFp values and clinical progression over time in a one-year follow-up period in individuals with SMCs. Additionally, Babiloni et al. [13] observed that both the TF and IAFp means were lower in the AD group than in the control group. Furthermore, low-frequency posterior alpha band activity (i.e., alpha2) and high-frequency posterior alpha activity (i.e., alpha3) were abnormally lower in the AD group, compared to the control group. This reduction in alpha2 and alpha3 spectral power, without specifying regions, was also observed in AD by Moretti et al. [14]. Previous studies using rsEEG recording in people with SMCs demonstrated that greater CR, compared to lower CR, was associated with higher temporal alpha 3 and lower posterior alpha 2 rhythms [15]. Additionally, the study conducted by Lopez et al. [16] found that higher CR was linked to increased parietal, occipital, and temporal alpha 2, as well as higher occipital alpha3 rhythms.

The aforementioned studies have shown that considering the individual basis when using TF and IAFp as markers can reveal additional information about individual neurophysiological characteristics. For this reason, the aim of this study was to investigate whether older people with SMCs, in comparison with controls, may present abnormal eyes-closed rsEEG posterior alpha rhythms around TF and IAFp. Based on the AD literature summarized previously, we tested the hypothesis that these differential features might be observed even in older people with SMCs [13,15,14]. We also analyzed how these parameters were modulated by sex. To the best of our knowledge, possible sex-related differences in people with SMCs have not yet been addressed. Finally, given that the participants in this study may be at risk for dementia-related disorders, and considering that a higher CR has been linked to greater tolerance for brain damage and reduced impact on cognitive manifestations [15,17], we explored the effect of CR on rsEEG.

2. Material and Methods

2.1. Participant

For this study, the sample recruited contained 82 participants. Eleven participants were excluded due to technical problems with their rsEEG records. The participants completed the Beck Depression Inventory-II (BDI-II; Beck et al.) [18], and three participants who scored above 20 were excluded from the analyses. Twenty is the cut-off point indicating moderate levels of depression, as reported [19] in a sample of Spanish participants. Consequently, the final sample employed was composed of 68 older adults (34 men, 34 women), all right-handed (Edinburg Handedness Inventory, [20]). The older people were recruited from La Nau Gran, a study program for people over 55 years old at the University of Valencia (Spain).

The exclusion criteria were: smoking >10 cigarettes a day; history of alcohol or drug abuse; having had surgery under general anesthesia during the past year; visual or hearing problems or the presence of an illness that involves an alteration of the nervous system; and/or a neurologic or psychiatric disorder. In addition, participants were also excluded if they were using any medication related to cognitive or emotional function, psychoactive substances, or beta-blockers, or if they had experienced a stressful event in the past six months. The participants who met the criteria were contacted by telephone and asked to attend two sessions that took place in the Laboratory of Social Cognitive Neuroscience of the University of Valencia (Spain).

The study was conducted according to the guidelines of the Declaration of Helsinki, and the Ethics Committee of the University of Valencia approved the study (Code: 1034878). All participants received verbal and written information about the study and voluntarily signed the informed consent prior to their participation.

Participants with unimpaired cognition (i.e., Mini Mental State Examination [MMSE] cut-off point superior to 27) were distributed into two groups according to their score on the Spanish adaptation [21] of the Memory Failures of Everyday questionnaire (MFE-30; [22]). This questionnaire contains 30 items about situations and activities of daily life, ranked on a 5-point Likert scale from 0 (never or almost never) to 4 (always or almost always). Twenty-one was the mean score obtained by the whole sample on the MFE-30 scale, as reported by Lozoya-Delgado et al. [21] in a sample of 900 Spanish participants. Therefore, based on this result and our previous study [23], participants who scored 21 or more comprised the SMCs group, and participants who scored less than 21 were included in the Control group. Remarkably, cut-off points and categorical distinctions are used in clinical procedures and may be helpful to neuropsychologists using this questionnaire.

There were no statistically significant group (SMCs vs. control) differences in sex ($\chi2$ (1)=2.885, p=.089), subjective socioeconomic status (SES) (t (66)=-1.394, p=.168) measured using the MacArthur Scale of Subjective Social Status [24], Body Mass Index (BMI) (t (66)=-.588, p=.559), MMSE (t (66)=-.517, p=.607), CR (t (66)= −1.809, p=.075), or educational level $\chi2$ (2)=5.546, p=.062). However, the SMCs group was marginally younger than the control group (t (66) =-1.972, p=.053). Descriptive data for the demographic measures are summarized in Table 1.

2.2. Procedure

Participants were tested individually. Upon arrival to the laboratory, the experimenter checked whether participants had followed the instructions offered previously, which were: abstain from heavy physical activity and sleep as long as usual the night before the recording; and refrain from consuming alcohol or any stimulant (i.e., caffeine, alcohol, cola, tea, or chocolate) and not eat or smoke for at least two hours before

Table 1
Characteristics of the sample (means and standard deviations).

Demographic measures	SMCs (n=35)	Control (n=33)	Men (n=34)	Women (n=34)
Sex (men/women)	14 m/21w	20 m/13w		
Age	63.3 (5.3)	65.9 (5.4)	65.5 (5.4)	63.8 (5.4)
SES	5.8 (1.6)	6.4 (1.6)	6.3 (1.6)	5.9 (1.5)
BMI	26.1 (5.4)	26.8 (3.6)	28.4 (3.8)	24.4 (4.5)
MMSE	28.8 (1.3)	29.0 (2.2)	28.7 (1.5)	29.1 (2.1)
CR	14.8 (3.4)	16.3 (2.7)	15.6 (2.8)	15.5 (4.0)
MFE-30	38.2 (11.7)	12.5 (5.9)	22.3 (13.7)	27.1 (17.4)
Educational level				
Primary	4 (5.7 %)	3 (4.5 %)	3 (4.4 %)	4 (5.9 %)
Secondary	15 (21.4 %)	6 (9.1 %)	8 (11.7 %)	13 (19.1 %)
University	16 (22.9 %)	24 (36.4 %)	23 (33.9 %)	17 (25 %)

Note. SMCs= subjective memory complaints; Control= no subjective memory complaints; m= men; w= women; SES= subjective socioeconomic status; BMI= body mass index; MMSE= Mini-Mental state examination; CR= cognitive reserve; MFE-30= Memory Failures of Everyday questionnaire

the session. Moreover, participants were instructed to drink only water.

Each participant completed two experimental sessions on two consecutive days, and half the participants attended in the morning (between 10.00 and 12.00 h) and the other half in the afternoon (between 15.00 and 19.00 h). On the first day, the participants completed the BDI-II, MFE-30, and CR tests. On the second day, the rsEEG session was carried out. The rsEEG activity was acquired while the participants were relaxed with their eyes closed and seated on a comfortable chair in a quiet and softly lit room. For each of the participants, the eyes-closed recording took three minutes. Instructions encouraged participants to sit quietly with relaxed muscles, no voluntary movement, and no talking. The participants did not have any difficulty following those instructions. An experimenter monitored the EEG traces in real time and verbally informed the participants whenever there were signs of behavioral or EEG drowsiness.

2.2.1. Cognitive Reserve (CR)

To measure the CR, the Cognitive Reserve Questionnaire [25] was used. It includes 8 items that measure various aspects of intellectual activity, such as: education, the educational level of the parents, the occupation carried out throughout life, musical training, knowledge of languages, and completion of training courses. In addition, it investigates the approximate frequency of cognitively stimulating activities related to lifestyle, such as reading habits and playing intellectual games. The maximum score is 25; the higher the score, the higher the cognitive reserve. A score of 6 or less is considered the lowest cognitive reserve. The reliability of the scale was estimated with the categorical omega coefficient ω_{NL} =.731 [26] in this sample.

2.2.2. Resting state EEG recording

EEG was recorded with a BrainAmp Standard amplifier system (Brain Products GmbH, Germany) from 29 electrode leads, according to the international 10–20 electrode system (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, FCz, M1, T3, T4, C3, Cz, C4, M2, P3, P4, Pz, P4, T5, T6, O1, Oz and O2) using an EEG elastic cap (Easycap, Falk Minow, Munich, Germany). We removed the two mastoid electrodes because they contained low-quality EEGs in many participants. Ground was placed at AFz. Data were referenced to FCz, and then the signals obtained were re-referenced to a common average of the remaining electrodes. Electrode-to-skin impedance was adjusted using electrolyte gel (SUPER-VISC High Viscosity Electrolyte-Gel, EasyCap, Brain Products GmbH), and it was kept below 5 kΩ before recording. Vertical and horizontal electro-oculograms were captured by additional electrodes (VEOG-, VEOG+, HEOG-, HEOG+) placed around the eyes to monitor eye movements. Signal preprocessing was performed offline with the BrainVision Analyzer 2.2 (Brain-Products, Germany).

The EEG was digitized in continuous recording mode for three minutes during eyes-closed conditions at a sampling rate of 500 Hz and after applying a bandpass filter between 0.3 Hz to 100 Hz. Blink artifacts were removed using Independent Component Analysis (ICA; [27]) and then visual inspection. Any segments containing artifacts other than eye blinks and movements were removed.

All previous conditioned data was transformed to the frequency domain through the Welch method obtaining the averaged Power Spectral Density. Time domain signal was segmented in 10 s length (5000 samples) with no overlapping, then each segment was masked with Hanning window, applied the corresponding variance correction and obtaining the Power Spectral Density using the FFT module built-in BrainVision Analyzer. By selecting the proper option, the output unit of this transformation is $\mu V^2/Hz$ with a resolution bandwidth of 0.1 Hz. Finally, averaging all frequency domain segments, one PSD representing the average power density of the full-length signal was obtained.

2.3. Estimation of Individual TF and IAFp

We calculated the TF as the frequency at the minimum power of the valley found in the theta frequency range. By contrast, IAFp was calculated as the frequency at the highest peak in the alpha range (see Fig. 1).

The TF and IAFp were computed for each subject involved in the study. To calculate these values, the spectrum for each participant was exported from the Brain vision analyzer to a text file. Then, each file was processed with Spyder IDE using python. The TF was calculated by searching for the first minimum at the left of IAFp. Then IAFp was found by searching for the global maximum within the alpha band. Finally, a visual inspection was carried out to avoid any outlier or mis-calculated values.

Based on TF and IAFp, we distinguished subregions of the alpha band frequency for each subject, lower (alpha1 and alpha2) and higher (alpha3) alpha bands, over five cortical regions of interest (ROI; see Fig. 1): frontal (F3, Fz, F4), central (C3, Cz, C4), temporal (T3, T4, T5, T6), parietal (P3, Pz, P4), and occipital (O1, Oz, O2), as follows: (i) alpha1 from TF to the central point of the TF-IAFp range, (ii) alpha2 from the central point of the TF-IAFp range to the IAFp peak, and (iii) alpha3 from this IAF peak to IAFp + 2 Hz.

The relative power density was computed for each alpha band as the ratio between the absolute and the mean power spectra from 2 to 40 Hz.

2.4. Statistics

Group and sex differences in demographic data were performed using *t*-tests and $\chi 2$ appropriately. Multivariate analyses of variance (ANOVA) were performed using *alpha frequency* indexes (TF and IAFp) in each region (parietal, occipital, and temporal) as a dependent variable, and *Group* (SMCs and control) and *Sex* (men/women) as independent variable. To test whether older people with SMCs, in comparison with controls, may present an abnormal eyes-closed rsEEG alpha band around TF and IAFp, repeated-measures ANCOVA were used, including the *Alpha Frequency Band* (alpha1, alpha2, and alpha3) and *ROI* (frontal, central, temporal, parietal, and occipital) as within-subject factors, *Group* and *Sex* as between-subject factors, and TF and IAFp as covariant variables, given that both are indexes of alpha frequency. In cases of violation of sphericity, Greenhouse-Geisser corrected values were reported. *Post hoc* comparisons were performed using Bonferroni correction. The partial eta squared coefficient (ηp^2) was used as a measure of effect size in the statistical analyses.

Finally, to test the possible association between CR and individual frequencies (TF and IAFp), we performed Pearsoń s partial correlations for each group, controlling for age to account for potential age-related effects [28]. Additionally, to evaluate the relationship between CR and frequency bands (alpha1, alpha2, alpha3), we also used Pearson's partial correlation. Given that a significant relationship was only observed in posterior areas in this sample, and that alpha waves are primarily produced during wakefulness over the posterior areas, correlations were conducted exclusively in these areas. The Bonferroni correction was applied to account for multiple comparisons, adjusting the significance level to 0.01 for the five correlations between individuals (TF and IAFp) and frequency alpha bands variables and CR.

Before performing the statistical analyses, for the alpha frequency markers, logarithmic transformation was applied to obtain values that followed a normal distribution. This procedure reduces inter-subject variability in the power estimates. CR was checked for normal distribution and homogeneity of variance using Kolmogorov–Smirnov. The Kolmogorov-Smirnov test confirmed that all the variables had a normal distribution ($p > .05$). For the statistical analyses, the level of significance was taken as <0.05. SPSS 26.0 was used to perform the statistical analyses.

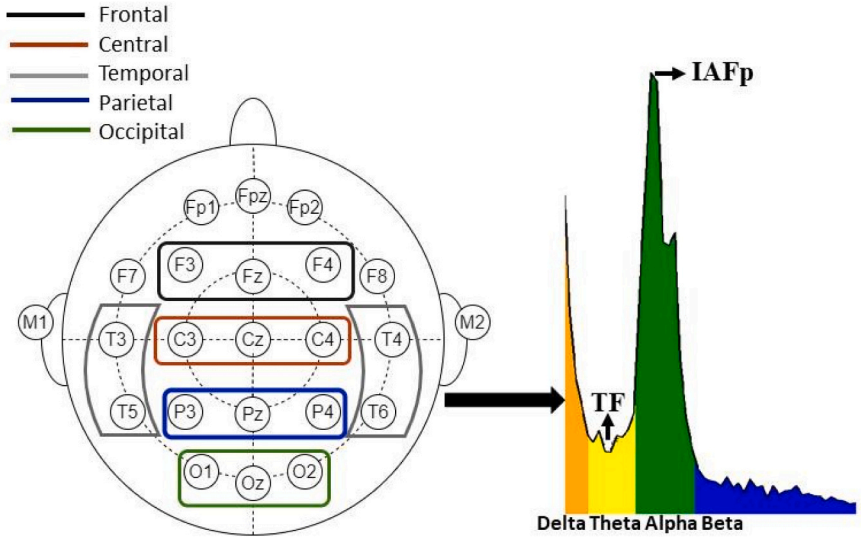

Fig. 1. Regions of interest used to study TF (transition frequency) and IAFp (individual alpha frequency peak) positioned according to the International 10–20 System.

3. Results

3.1. Alpha indexes: TF and IAFp

For the TF, the analyses revealed that Group [$F(1,58)=.003$, $p=.960$, $\eta p^2=.050$], Sex, [$F(1,58)=.001$, $p=.993$, $\eta p^2=.050$], and the Group*Sex interaction [$F(1,58)=.137$, $p=.713$, $\eta p^2=.065$] were not significant. Similarly, for IAFp, the Group [$F(1,58)=.413$, $p=.523$, $\eta p^2=.097$] and Sex [$F(1,58)=.000$, $p=.984$, $\eta p^2=.050$] factors and the Group*Sex interaction [$F(1,58)=.532$, $p=.460$, $\eta p^2=.111$] did not reach significance (Table 2).

3.2. Alpha Frequency band

Results showed that the Alpha Frequency Band*Sex [$F(2,100)=6.545$, $p=.002$, $\eta p2=.116$], Alpha Frequency Band*Group*Sex [$F(2,100)=4.539$, $p=.013$, $\eta p^2=0.083$], and Alpha Frequency Band*Group*Sex*ROI [$F(8,448)=1.951$, $p=.020$, $\eta p^2=0.039$] interactions were significant. *Post hoc* analyses revealed that men showed higher alpha1 ($p=.005$) and lower alpha3 frequency ($p=.016$) compared to women. Additionally, women with SMCs exhibited lower alpha3 frequency compared to control women ($p=.029$), particularly in parietal regions ($p=.037$) (Fig. 2).

No other main effects (all $ps>.763$) or interactions reached statistical significance (all $ps>.910$).

Table 2
Mean values of alpha indexes (TF/IAFp).

	Alpha indexes	SMCs	Control	Men	Women
TF	FR	6.75 (1.25)	6.48 (1.17)	6.67 (1.10)	6.58 (1.31)
	CR	6.40 (1.24)	6.42 (0.99)	6.43 (1.24)	6.37 (1.01)
	TR	6.42 (1.38)	6.19 (1.10)	6.26 (1.21)	6.34 (1.30)
	PR	6.14 (1.09)	6.25 (0.85)	6.16 (0.80)	6.18 (1.11)
	OR	6.30 (1.18)	6.12 (0.97)	6.12 (0.99)	6.29 (1.16)
IAFp	FR	9.70 (1.24)	9.58 (0.97)	9.75 (1.08)	9.55 (1.13)
	CR	9.75 (1.19)	9.46 (0.85)	9.51 (1.02)	9.69 (1.07)
	TR	9.67 (1.22)	9.52 (0.83)	9.61 (1.04)	9.59 (1.06)
	PR	9.81 (1.14)	9.26 (0.82)	9.71 (0.97)	9.72 (1.03)
	OR	9.79 (1.15)	9.74 (1.22)	9.84 (0.91)	9.70 (1.08)

Note. SMCs= subjective memory complaints; Control= no subjective memory complaints; TF= theta/alpha transition frequency; IAFp= individual alpha frequency peak; FR= frontal region; CR= central region; TR= temporal region; PR= parietal region; OR= occipital region.

3.2.1. Correlations between CR and alpha indexes and alpha frequency bands

Partial Pearson's correlations indicated that CR negatively correlated with IAFp ($r=-.468$, $p=.005$) only in the SMCs group, whereas these associations did not appear in the control group (all $p>.799$) (Table 3). No other associations were observed (all $p>.922$) (Table 3).

4. Discussion

In this study, rsEEG power density at the individual low alpha band (alpha1 and alpha2) and high alpha band (alpha3) was investigated in older people with SMCs and controls, and the importance of sex was examined. In addition, in each group (SMCs vs control), correlation analyses were performed between CR and both alpha indexes (TF and IAFp) and the posterior alpha band. Summarizing the main findings, we did not find group or sex differences in the two alpha indexes. However, the SMCs group, in comparison with the control group, showed a reduction in alpha3 power. More specifically, women with SMCs displayed a significant decrease in alpha3 power, compared to control women, particularly in the parietal region. Apart from the group, men showed higher alpha1 and lower alpha3 than women. Finally, only in people with SMCs, a greater CR was associated with slowing IAFp.

The hypothesis that the alpha indexes of people with SMCs are slower when compared with a control population could not be confirmed in our sample. In contrast, previous studies reported a slower IAFp mean in MCI [29] and AD [14,30]. This finding of IAFp slowing in neurodegenerative disorders might be explained by a slowing or reorganization of the oscillatory sources in the theta-alpha frequency [29]. One might assume that the lack of significant differences between SMCs and control people in our study may be due to the high stability of alpha indexes in individuals with no pathology [31]. Therefore, these alpha indexes could be affordable biomarkers for assessing disease status or progression. Future longitudinal studies should test this using the current methodological approach.

In this study, the SMCs group showed lower alpha3 power compared to the control group, with a notable trend of decreased posterior alpha3 observed only in women. This decrease in power is seen as evidence of the cholinergic system's role in modulating alpha rhythms, given the well-documented acetylcholine deficit in the earliest stages of AD [32]. From a physiological point of view, the low alpha frequency band (alpha1 and alpha2) is mainly related to thalamo-cortical synchronization and a vigilance state, whereas the high alpha frequency band

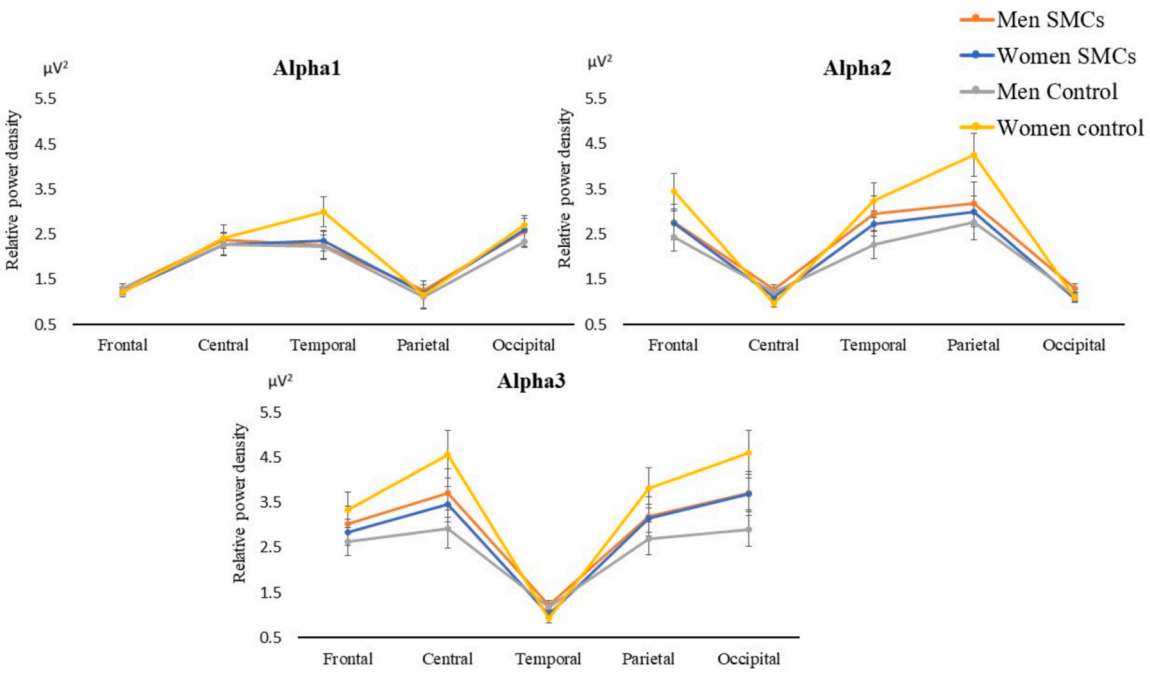

Fig. 2. Relative band power (alpha1, alpha2, alpha3) in five regions of interest (frontal, central, temporal, parietal, and occipital) in both groups (SMCs and control) and sex.

Table 3
Correlations between CR and alpha indexes and bands in older people in both groups.

	SMCs CR	Control
PR-TF	r= −.205, *p*=.245	r = −.047, *p*=.799
PR-IAFp	**r= −.468, *p*=.005**	r = −.242, *p*=.181
PR alpha1	r=.022, *p*=.902	r =.081, *p*=.659
PR alpha 2	r=.392, *p*=.022	r =.018, *p*=.922
PR alpha 3	r=.223, *p*=.205	r =.051, *p*=.780

Note. SMCs= subjective memory complaints; Control= no subjective memory complaints; CR= Cognitive Reserve; PR-TF= parietal region transition frequency; PR-IAFp= parietal region individual alpha frequency peak; PR= parietal region.

(alpha3) is related to corticocortical synchronization [10]. Thus, the findings of this study seem to be consistent with previous evidence showing that a cholinergic deficit usually affects the synchronization mechanism at the base of the alpha power, which is modulated by corticocortical interaction [14]. More specifically, our results suggest that the slowing in higher alpha power is modulated by sex, which merits further attention.

Regardless of the group, men showed higher alpha1 and lower alpha3 than women. Sex differences in the alpha rhythms in the healthy population have been reported with mixed results. On the one hand, it was reported that, compared to women, men showed lower alpha rhythms [33]. On the other hand, higher power in lower and high alpha was observed in women compared to men [34]. However, these studies did not consider individual variations in peak alpha frequency in alpha rhythms as this study did. Therefore, the higher alpha1 observed in this study could be attributed to an increase in the internal control of attention, whereas the lower alpha3 could be the result of desynchronization in cortical areas when cognitive demands arise [10].

As a novelty, here we reported that a greater CR was associated with a slowing of IAFp in older people with SMCs. This relationship might indicate a compensatory and protective mechanism of the CR to maintain brain function. The compensatory mechanisms of CR may attenuate the linear relationship between functional brain integrity and cognitive status in older people with SMCs. However, when CR is depleted, cognitive changes become evident, leading to a rapid decline in cognitive status [15,35]. Furthermore, the compensatory mechanism of CR has been associated with increased indicators of brain pathology, such as reduced brain metabolism, increased amyloid deposition, or increased rates of atrophy [17]. Our findings propose that this higher CR is associated with an enhanced brain capacity for sustaining cognitive function. In this vein, Lopez et al. [16] demonstrated that higher educational (a proxy for CR) attainment is associated with a delayed onset dementia in healthy older adults. Similarly, a previous magnetic resonance imaging study showed that older people with a high educational level were more likely to resist the damaging effects of severe white matter lesions, whereas a severe white matter lesion load increased the risk of transition to MCI/dementia in people with a low educational level [36]. Therefore, it is important to note that an elevated CR may enhance resilience to neurodegeneration and potentially mask neurological diseases such as dementia. Because this is a cross-sectional study, we could not experimentally examine the compensatory hypotheses by following the evolution of the participants' clinical status over time. In this paper, we use theoretical constructs to elucidate the observed effects on rsEEG alpha rhythms, based on findings from the referenced literature.

In conclusion, the findings presented provide an important complement to the literature reporting high stability of TF and IAFp in the absence of pathology, as shown by older people with SMCs. This suggests that substantial changes in these parameters might be indicative of a pathological process [37]. However, the decrease in alpha3 activity, such as the one observed in older women with SMCs, shows an initial rsEEG change. Incorporating individual EEG frequency estimation into diagnostic research protocols could offer a promising and cost-effective approach for AD diagnosis. However, it is crucial to adhere to the latest clinical neurophysiology guidelines and thoroughly assess the evidence, considering both limitations and recommendations, before drawing conclusions about the diagnostic potential of EEG for AD. Finally, the compensatory effect of CR seems to interact with neurophysiological mechanisms generating cortical alpha rhythms. A larger sample size and current analyses of functional brain changes would be needed to confirm these findings. Additionally, longitudinal follow-up studies could aid in understanding the evolution of these parameters, particularly in

exploring the compensatory effects of CR. Such studies could shed light on whether individuals with higher CR maintain healthy cognitive functioning over extended periods compared to those with more limited premorbid cognitive resources.

Conflict of interest

No potential conflict of interest was reported by the authors.

CRediT authorship contribution statement

Alicia Salvador: Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Conceptualization. **Vanesa Hidalgo:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Vanesa Perez:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors did not use generative AI technologies in the preparation of this paper.

Data Availability

Data will be made available on request.

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