

EEG markers and subjective memory complaints in young and older people

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ABSTRACT

Subjective memory complaints (SMCs) have been related to subtle cognitive deficits and neural changes. In this study, we investigated whether EEG rhythms, usually altered in mild cognitive impairment and Alzheimer's disease, are also affected in SMCs compared to people without SMCs. Seventy-one older adults (55–74 years old) and 75 young people (18–34 years old) underwent 3 min of EEG recording in a resting-state condition with their eyes open (EO) and eyes closed (EC) and a comprehensive neuropsychological evaluation. The EEG measures included were power spectral delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (13–30 Hz), and EEG reactivity to EO. Compared to controls, older people with SMCs showed increased theta power and a loss of alpha reactivity to EO. Additionally, in older participants with SMCs, the theta power spectral was related to deficits in verbal memory. In contrast, we failed to find differences in the young people with SMCs, compared to the control group, in the power spectral or the EEG reactivity to EO. Our findings suggest that neurophysiological markers of brain dysfunction may identify cognitive changes even before they are observed on objective neuropsychological tests, at least in older people.

1. Introduction

The identification of the earliest signs of dementia, along with the possibility of early prevention and interventions to slow its progression, has led to great interest in subjective memory complaints (SMCs). SMCs have been conceptualized as subjective awareness of memory loss in the absence of any organic condition (Abdulrab and Heun, 2008). This definition was later revised to refer to a self-perception of decline in cognitive capacities in any cognitive domain (not only memory performance) (Jessen et al., 2014, 2020). Nevertheless, SMCs are the main feature of subjective cognitive decline and the most common at all ages (Begum et al., 2013; Sohrabi et al., 2018). In fact, previous studies in older people have found that SMCs are predictive of a high risk of later cognitive decline and the development of neurodegenerative disorders (Glodzik-Sobanska et al., 2007; Jessen, 2010; Roh et al., 2011; Rönnlund et al., 2005). Thus, understanding the mechanisms underlying SMCs is crucial in order to develop early detection strategies.

Some studies have observed a relationship between SMCs and worse

performance on objective neuropsychological tests (Hohman et al., 2011; Peter et al., 2014), although this association has not always been found (Balash et al., 2012). A possible reason for this discrepancy could be the different methods used to measure memory complaints (i.e., a simple question, set of questions or criteria, etc.) (Abdulrab and Heun, 2008; Jessen et al., 2014) and the fact that the standard memory tests used might not be sensitive enough to identify subtle memory difficulties (Abdulrab and Heun, 2008). Subtle changes in cognitive functioning can hardly be detected in neuropsychological evaluations. However, neuroimaging studies have shown that older people with SMCs, compared to controls, have significantly smaller brain structures, which have been found to be affected early in neurodegenerative processes (Hafkemeijer et al., 2013; Flier et al., 2004; Striepens et al., 2010), and increased functional connectivity, which has been explained as a greater cognitive effort to compensate for losses in cognitive function (Hafkemeijer et al., 2013). These findings suggest that SMCs can be part of the temporal sequence of cerebral changes preceding mild cognitive impairment (MCI) or Alzheimer's disease (AD) (Galluzzi and Frisoni, 2008).

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The use of electroencephalography (EEG), a non-invasive technique, in people with SMCs, a population with a higher risk of developing dementia, may offer crucial information to develop markers of early cognitive decline and delay or prevent progression to MCI or AD. EEG is characterized by a high temporal resolution (<1 ms), which is ideal for studying the different frequency spectrums (Babiloni et al., 2016; Biasucci et al., 2019). In this vein, EEG recording during resting conditions with eyes open (EO) and eyes closed (EC) could be an important tool to evaluate oscillatory signals such as spectral power. Investigating the changes from EC to EO, called EEG reactivity, in people with SMCs might be promising as well (Alexander et al., 2006; Babiloni et al., 2006, 2020). The power spectral is proportional to the rate of energy change at a specific frequency or frequency band (Lejko et al., 2020). Frequency bands range from slow (delta and theta) to fast (alpha, beta, and gamma) (Lejko et al., 2020). EEG reactivity is known as the effect of alpha desynchronization with the processing of visual stimuli (Alexander et al., 2006). Additionally, the recording of the EEG rhythms at rest does not induce the fatigue or anxiety typically associated with task performance (Babiloni et al., 2016).

Previous investigations have used EEG recordings to demonstrate power spectral changes in people with MCI or AD (see review: Lejko et al., 2020). Studies in these populations reported an increment in delta and theta power and a decrease in beta power in early phases of AD, followed by a decrease in alpha power in later stages of AD (Babiloni et al., 2012; Babiloni et al., 2006; Hatz et al., 2013; Roh et al., 2011; Michels et al., 2017). When investigating EEG reactivity, the differences seem to be limited to alpha bands. In patients with AD, alpha reactivity was found to be lower than in control groups (Schumacher et al., 2020). However, these differences were not observed in patients with MCI (Fröhlich et al., 2021). In the case of SMCs, Alexander et al. (2006) observed an increased alpha power in EO and EC, as well as increased frontal beta power and theta power only in EC conditions. Gouw et al. (2017) showed that people with SMCs with amyloid positivity had intermediate spectral values between stable people with SMCs and people with MCI. Specifically, they found a higher relative power in the delta and theta bands and a higher relative power in the alpha band. Regarding EEG reactivity, whereas some studies did not observe differences in EEG reactivity in SMCs (Alexander et al., 2006), using synchronization likelihood, Pijnenburg et al. (2008) found a loss of reactivity in people with SMCs.

Although SMCs are commonly reported by older people (Glodzik-Sobanska et al., 2007; Markova et al., 2017), they are also observed in young adults (Derouesné et al., 1999; Ginó et al., 2010; Loprinzi, 2019; Mendes et al., 2008). Population-based studies suggest that the prevalence of SMCs increases over time, and that up to 6.3 % of young people and 10.5 % of older people report some form of perceived difficulty in cognitive functioning (Begum et al., 2013). Regarding cognitive performance, as observed in older people, SMCs have been associated with worse objective cognitive performance in some but not all of the studies in young adults (Montenegro et al., 2013; Ruiz-Sanchez de Leon et al., 2010). However, no research has investigated EEG markers during resting state conditions in young adults with SMCs.

In sum, few studies have compared the EEG resting state in people with SMCs and controls, and the results obtained in older people have been inconsistent. In addition, this topic has been underexplored in young people with SMCs. Therefore, using EEG registration with EO and EC, we investigated the spectral power of frequency bands and EEG reactivity in older and young people with and without SMCs. Moreover, we sought to determine whether there is a correlation between the region and specific spectral powers and EEG reactivity and neuropsychological measures. We tested three main hypotheses. The first hypothesis was that the cortical EEG rhythms usually altered in MCI and AD (i.e., decrease in fast EEG waves and increase in slow waves) would also be affected in SMCs, compared to controls, as a possible early marker of underlying pathological processes (Alexander et al., 2006; Babiloni et al., 2010). The second hypothesis was that EEG reactivity would be

similar in all the frequency bands in both groups (SMCs and control), based on previous findings (Alexander et al., 2006; Fröhlich et al., 2021). Finally, an alteration in resting EEG would be related to worse cognitive function (Babiloni et al., 2012; Gaubert et al., 2019).

2. Material and methods

2.1. Participants

Eighty-three older adults and 82 young adults were recruited for this study. Three older participants were excluded due to incomplete data. Six older participants and four young participants were also excluded due to technical problems. All the participants completed the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), and three older participants and three young participants who scored above 20 were excluded from the analyses. Consequently, the final sample was composed of 146 right-handed participants (71 older adults: from 55 to 75 years of age, 35 men and 36 women; 75 young people: from 18 to 34 years of age, 38 men and 37 women).

Participants were distributed into two groups according to their scores on the Spanish adaptation (Lozoya-Delgado et al., 2012) of the modified version of the Memory Failures of Everyday (MFE-30) questionnaire (Sunderland et al., 1984). This questionnaire contains 30 items about situations and activities of daily life, rated on a 5-point Likert scale ranging 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. Thus, participants who scored above 21 comprised the SMCs group, whereas participants who scored equal to or below 21 were included in the Control group. The mean score obtained by the sample as a whole on the MFE-30 scale was 21, and the median was 20. In addition, Lozoya-Delgado et al. (2012) observed that 21 was the mean score on this questionnaire in a sample of 900 Spanish participants. It is worth noting that cut-off points and categorical distinctions are used in clinical procedures and may be helpful to neuropsychologists using this questionnaire. Partial results from the older subsample have been previously reported (Garrido-Chaves et al., 2021; Perez et al., 2021).

Both older and young participants were recruited via advertisements and informative talks at the University of Valencia campus (Spain). Most of the older participants were recruited in classes of La Nau Gran, a study program for people over 55 years old. Most of the young people were college students from different areas, and the rest were referred by these participants (acquaintances, relatives, or friends).

The exclusion criteria were: smoking >10 cigarettes a day; history of alcohol or drug abuse; having had surgery under general anesthesia in the past year; visual or hearing problems; or any illness that involves an alteration of the nervous system or a neurological or psychiatric disorder. In addition, participants were 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.

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

2.2. Procedure

Each participant attended two individual sessions on two consecutive days. Sessions lasted approximately 2 h in the morning (between 10.00 and 12.00 h) or in the afternoon (between 15.00 and 19.00 h). Half the participants attended in the morning and the other half in the afternoon. There were no differences in the number of older ($t_{(68)} =$

–0.711, $p = .480$) and young ($t(73) = -0.446$, $p = .657$) participants in each group in each shift. Each participant started both sessions at the same time of day. The first session consisted of a neuropsychological assessment, and the second session consisted of an EEG recording.

In each session, the experimenter checked whether participants had followed the instructions given previously, which were: abstain from heavy physical activity and sleep as long as usual the night before the recording; refrain from consuming alcohol or any stimulant (i.e., caffeine, alcohol, cola, tea, or chocolate); and avoid eating or smoking for at least 2 h before the experimental session. Moreover, participants were instructed to drink only water.

2.2.1. Session one: neuropsychological assessment

In the first session, the weight and height of the participants were measured. In addition, participants completed the MFE-30 questionnaire, a General Questionnaire with demographic data, and a battery of eleven neuropsychological tests evaluating the following cognitive domains.

2.2.1.1. Verbal memory. It was assessed using the Spanish version of the Free and Cued Selective Reminding Test (FCSRT; (Peña-Casanova et al., 2009), which consists of a preliminary list of 16 words where the subject has to identify each word when answering a question (e.g., *which one is a bird?*). Then, the distracting task starts, where the participant has to subtract numbers by 3 for 20 s. After that, the free recall begins and lasts for 90 s. In the facilitated recall, the experimenter asks the participant the facilitating questions about the word that he/she did not remember in the free recall part. The same process is repeated in three trials. Five indexes were obtained for this task: (a) free recall on the first trial, with a maximum score of 16 points; (b) total free recall: the sum of free recall on the three trials, with a maximum score of 48 points; (c) total recall: the sum of total free recall and total facilitated recall, with a maximum score of 48; (d) free delayed recall: the sum of total free delayed recall, with a maximum score of 16 points; and (e) total delayed recall: the sum of total free deferred recall and facilitated deferred recall, with a maximum score of 16 points.

2.2.1.2. Attention and working memory. It was evaluated with the Digit Span Test from the Wechsler Memory Scale (Wechsler, 1997). This task consists of two subtests: (a) Digit Span Forward (DS-Forward) and Digit Span Backward (DS-Backward). DS-Forward is a measure of attention and memory span. The participants listened to numbers and had to repeat them in the same order. DS-Backward was used as a measure of the executive component of working memory, and the participants repeated the numbers they had previously heard in the reverse order. On this task, the sequences start at Level 2 and can increase to Level 8. Participants have two chances for each sequence length; if they are successful on one of the sequences, the next sequence begins.

2.2.1.3. Visuo-spatial working memory. To measure visuo-spatial working memory, the Automated Working Memory Assessment (AWMA) was used (Alloway et al., 2008). On the Dot Matrix Forward subtest, the participants pointed at the red dots in the same order they appeared. The Dot Matrix Forward subtest measures attention and memory span. On the Dot Matrix Backward subtest, the participants pointed at the boxes in the reverse order to the way they appeared. This subtest is a measure of the executive component of working memory. Two outcomes were acquired: (a) Dot Matrix-Forward: total number of correct trials in the same order; and (b) Dot Matrix-Backward: total number of correct trials in the reverse order. On this task, the scores range between 2 and 8. Participants have two chances for each sequence length; if one of the sequences is performed correctly, the next sequence starts.

2.2.1.4. Attention-switching. The Trail-Making Test (TMT) was used to examine attention-switching. It consists of two trials, TMT-A and TMT-B

(Reitan, 1992). Each trial was composed of circles distributed on a white sheet of paper. On TMT-A, the circles were numbered from 1 to 25, and the participants were asked to trace a line connecting them in increasing order as quickly as possible. TMT-B includes circles numbered from 1 to 13 and circles with letters from A to L. Participants were asked to trace a path for the circles in order, alternating from a number to a letter. Two outcomes were obtained: (a) TMT-A: total time needed to finish Part A, and (b) TMT-B: total time needed to finish Part B.

2.2.1.5. Interference control. Stroop Color-Word Interference was used to examine the effects of interference on reading ability (Golden, 1978). This task contains three parts: (a) word page: the names of colors printed in black ink (W); (b) color page: lines of Xs printed in colored ink (C); and (c) word-color page: the word meanings and ink colors do not match (WC). Participants were asked to look at each sheet and move through the columns, reading the words or naming the colors of the ink as quickly as possible for 45 s. Three scores, as well as an interference score, are generated using the number of items completed on each page, with higher scores reflecting less interference in reading ability. Subsequently, the WC' was calculated: $WC' = (W \times C) / (W + C)$. Finally, the Stroop Interference outcome was obtained (Stroop Interference = $WC - WC'$), which is a measure of the ability to inhibit an automatic response.

2.3. Verbal fluency

To measure phonological fluency, participants were asked to produce as many words as possible in order to assess phonological and semantic fluency. For phonological fluency, participants were asked to generate as many words as possible beginning with the letters F, A, and S. For semantic fluency, participants were asked to generate as many words in the animal category as possible. Sixty seconds were allowed for each category. Only correct answers were scored, intrusions or repeated attempts were not considered, and variations within the same species were not counted. Instructions were given following the administration procedures provided in the Barcelona test (Peña-Casanova, 1991).

2.3.1. Session two: resting state with EEG recording

Using an EEG cap (EasyCap, Falk Minow, Munich, Germany), EEG was recorded from 29 electrode positions according to the 10-20 System (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, FCz, M1, T3, C3, Cz, C4, M2, P3, P4, Pz, P4, T5, T6, O1, Oz and O2), with a BrainAmp Standard amplifier system (Brain Products GmbH, Germany). Data were referenced to FCz, and then the signals obtained were re-referenced to a common average of the remaining electrodes. To monitor eye movements, vertical and horizontal electro-oculograms were captured by additional electrodes (VEOG-, VEOG+, HEOG-, HEOG+) placed around the eyes. Electrode-to-skin impedance was reduced using electrolyte gel (SUPER-VISC High Viscosity Electrolyte-Gel, EasyCap, Brain Products GmbH), and these were kept below 5 k Ω . The bandpass filter was set at 0.3–100 Hz with a sampling rate of 500 Hz. All data were digitized in continuous recording mode for 3 min during each of the EO and EC conditions. We removed the two mastoid electrodes because they contained low-quality EEG in many participants. Participants were seated in a comfortable chair in a quiet and dimly lit room. Participants were asked to sit quietly with both hands resting comfortably on the table in front of them. They looked at a fixation cross at the center of a computer screen for 3 min (condition EO) and then closed their eyes for 3 min (condition EC). This order of recording was constant for each participant in this study. To maintain a constant level of alertness, an experimenter controlled the EEG traces online and verbally informed the participants whenever there were signs of behavioral or EEG drowsiness.

2.4. Spectral analysis of the EEG data

The standard frequency bands of interest in the EEG source analyses

were: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (13–30 Hz), based on previous studies of resting EEG rhythms in pathological aging (Babiloni et al., 2020). The gamma band was excluded from the analysis because the signal in this band is usually altered by muscle artifacts (Whitham et al., 2007). We estimated the average power spectral density for each band in each resting condition (EO, EC). Each three-minute epoch was divided into adjacent intervals of 2 s. Power spectral analysis was performed by applying a Fast Fourier Transform (FFT). The electrodes were grouped in five cortical regions of interest (ROI): the frontal (F3, Fz, F4), central (C3, Cz, C4), parietal (P3, Pz, P4), occipital (O1, O2), and temporal (T3, T4, T5, T6) regions. Power spectral density was log-transformed prior to statistical analysis.

In addition, we considered EEG reactivity to EO, which was calculated separately for each frequency band by subtracting the logarithm of the power of EO for each ROI from the logarithm of the power in each band of EC.

2.5. Statistics

To investigate differences between groups (SMCs vs. Controls) on demographic data and neuropsychological data, Student's *t*-tests were performed, except in the cases of educational level and sex, which were investigated using χ^2 .

Independent repeated-measures ANOVAs were used to test the first hypothesis (i.e., compare regional spectral power variables among groups). All EEG power density distributions were processed by logarithmic transformation and retested. For spectral power analyses, *Group* (SMCs and control) served as the between-subject factor, and *Frequency band* (delta, theta, alpha, and beta), *ROI* (frontal, central, parietal, occipital, and temporal), and *Condition* (EO and EC) served as within-subject factors. To examine the second hypothesis (i.e., whether EEG reactivity was similar in all the frequency bands), we used independent repeated-measures ANOVA with two within-subject factors, *Frequency band* (delta, theta, alpha, and beta) and *ROI* (frontal, central, parietal, occipital, and temporal), and one between-subject factor, *Group* (SMCs vs. control). All analyses were carried out separately in young and older adults to avoid reducing the statistical power. In the case of violation of sphericity, Greenhouse-Geisser corrected values were reported. Post hoc comparisons were performed using Bonferroni correction.

Finally, to test the third hypothesis, we examined the possible relationships between neuropsychological test scores and spectral power and EEG reactivity when significant differences were found between groups (SMCs and control). Pearson's correlations were used to analyze the relationships between these variables and neuropsychological performance. To limit the number of variables, we performed an exploratory factor analysis using Oblimin direct with the final sample (i.e., 146 participants). Three factors were identified: (I) verbal memory, which explained 37.5 % of the total variance; (II) executive function, which explained 14.5 %; and (III) attention, which explained 9.8 % (total variance explained: 61.8 %). The Kaiser–Meyer–Olkin (KMO) indicated a satisfactory relationship between sample size and the number of variables (0.817), and Bartlett's test indicated that the correlations between variables were sufficient to warrant a factor analysis, $C^2(91) = 955.418$, $p < .001$. The verbal memory factor included: free recall on the first trials; total free recall; free delayed recall; and total delayed recall indexes from the FCSRT. Executive function was tested with the DS-Forward, DS-Backward, Dot Matrix, Backward Dot Matrix, and Stroop Interference. Attention was tested with the TMT-A, TMT-B, Semantic fluency, Phonetic fluency.

Before performing the statistical analyses, dependent variables in the ANOVA and neuropsychological test scores were 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.

3. Results

3.1. Demographic variables and neuropsychological performance

In both age groups, there were no differences between the SMC and control groups in sex ($\chi^2 = 0.67$, $p = .443$), educational level ($\chi^2 = 0.278$, $p = .455$), or subjective socioeconomic status (SES) ($t_{(144)} = -1.598$, $p = .112$), measured using the MacArthur Scale of Subjective Social Status (Adler et al., 2000). However, the Body Mass Index (BMI) was higher in older people than in young people ($t_{(143)} = -6.622$, $p = .001$). Descriptive data for the demographic measures are summarized in Table 1.

In older people, results revealed that free recall scores on the first trial ($t_{(65)} = -2.211$, $p = .031$) and total recall scores ($t_{(65)} = -2.059$, $p = .044$) on the FCSRT and DS-Forward ($t_{(64)} = -2.921$, $p = .005$), were lower in SMCs than in the control group. No statistically significant differences were found on any other neuropsychological measures (all $p > .816$). However, the group means confirm that the older people with SMCs were within the normality range of the population.

In young people, results revealed that free recall on the first trial ($t_{(70)} = -2.443$, $p = .017$), total free recall ($t_{(70)} = -2.927$, $p = .005$), and total delayed recall ($t_{(70)} = -2.288$, $p = .035$) on the FCSRT test were

Table 1

Means (and standard deviations) of demographic and neuropsychological data.

Demographic measures	Older group $n = 71$		Young group $n = 75$	
	SMCs ($n = 34$)	Control ($n = 37$)	SMCs ($n = 40$)	Control ($n = 35$)
Sex	13m/21w	22m/15w	19m/21w	19m/16w
Age years	63.8 (5.6)	65.6 (5.3)	21.3 (3.3)	22.8 (3.6)
BMI (kg/m ²)	26.6 (4.6)	26.4 (3.5)	22.3 (3.6)	22.4 (3.0)
SES	6.0 (1.3)	6.2 (1.3)	5.7 (1.1)	5.8 (1.1)
Educational level				
Primary	5 (7.3 %)	3 (4.0 %)		
Secondary	13 (19.1 %)	10 (13.5 %)	33 (41.2 %)	18 (25.2 %)
University	16 (23.5 %)	24 (32.4 %)	7 (8.7 %)	15 (21.4 %)
Neuropsychological measures				
Free recall of the first trial	7.66 (2.15)	8.73 (1.97)	8.83 (2.64)	10.28 (2.37)
Total free recall	28.70 (6.30)	31.62 (6.40)	33.0 (4.96)	36.22 (4.35)
Total recall	42.86 (5.02)	45.05 (3.66)	45.16 (4.33)	46.37 (2.22)
Free delayed recall	11.13 (2.48)	11.70 (2.65)	13.35 (1.43)	14.14 (1.49)
Total delayed recall	15.20 (1.49)	15.48 (0.93)	15.70 (0.61)	15.74 (0.50)
DS-Forward	5.65 (0.81)	6.29 (0.93)	6.70 (0.90)	6.91 (1.01)
DS-Backward	4.24 (0.98)	4.35 (1.00)	5.83 (0.95)	5.65 (1.34)
TMT-A	45.60 (14.78)	46.67 (17.01)	36.62 (13.63)	32.97 (11.17)
TMT-B	95.60 (48.15)	83.48 (29.41)	70.78 (27.44)	64.10 (24.44)
Dot Matrix	4.37 (0.94)	4.72 (0.87)	6.18 (0.73)	5.94 (1.25)
Backward Dot Matrix	4.31 (1.03)	4.37 (1.08)	5.40 (0.89)	5.40 (1.16)
Stroop Interference	-1.16 (7.06)	-1.56 (6.90)	8.48 (7.77)	10.82 (9.76)
Semantic fluency	40.20 (9.37)	40.56 (9.37)	38.67 (9.67)	40.40 (10.64)
Phonetic fluency	21.26 (6.88)	22.56 (7.42)	21.62 (5.14)	22.20 (5.51)

Note. Significant differences are displayed in bold. Abbreviations: SMCs = subjective memory complaints; Control = no subjective memory complaints; m = men; w = women; BMI = body mass index; SES = subjective socioeconomic status; TMT: Trail Making Test.

lower in SMCs than in the control group. Young people with SMCs were also within the normal range of the population. No differences were obtained on any neuropsychological measures (all $p > .764$). Descriptive data for the neuropsychological variables are summarized in Table 1.

3.2. Spectral power

In older people, the main effect of Frequency band, $F(2.324, 141.743) = 324.866, p < .001, \eta^2 = 0.045$, and Condition, $F(1, 61) = 42.144, p < .001, \eta^2 = 0.409$, as well as the Frequency Band * Condition * Group interaction, $F(2.744, 167.399) = 2.864, p = .043, \eta^2 = 0.045$, were statistically significant. Post hoc analyses revealed that older people with SMCs showed greater theta power in the EO condition ($p = .035$), but not in the EC condition ($p = .063$), compared to controls (see Fig. 1).

In young people, the main effects of Frequency band, $F(1.894, 132.592) = 471.177, p < .001, \eta^2 = 0.871$, and Condition, $F(1, 70) = 47.225, p < .001, \eta^2 = 0.403$, were significant. However, the Frequency Band * Condition * Group interaction was not significant, $F(2.398, 167.893) = 1.433, p = .240, \eta^2 = 0.020$ (see Fig. 2).

3.3. EEG reactivity

In older people, the Frequency Band * ROI * Group interaction was significant, $F(12, 732) = 2.004, p = .022, \eta^2 = 0.032$. Post hoc analyses revealed that older people with SMCs showed a reduction in central alpha reactivity ($p = .046$) compared to older control people. Other comparisons of ROI reactivity scores across theta, beta, and delta were not significant (all $p > .984$). Young people with SMCs did not show significant effects of any factors or their interactions (all $p = .505$).

3.4. Relationships between neuropsychological performance and spectral power

Table 2 shows the relationships between theta power and alpha reactivity and neuropsychological measures related to verbal memory,

executive function, and attention. In older people with SMCs, in the EO condition, positive correlations were found between: factor (I) verbal memory and central theta power ($r = 0.365, p = .047$). The rest of the ROI did not correlate significantly with any cognitive function in the EO conditions for SMCs or control older people ($p > .985$). Regarding EEG reactivity, in older people with SMCs and controls, central alpha reactivity did not correlate significantly with any cognitive function ($p > .985$).

4. Discussion

In the present study, we examined whether cortical EEG rhythms, commonly altered in MCI and AD, are also affected in young and older people with SMCs. Summarizing the main findings, overall performance on the cognitive tests was similar in older people with SMCs and younger people with SMCs, with the following exceptions. Older people with SMCs obtained lower scores on free recall on the first trial and on total recall on the FCSRT and DS-Forward. Young people with SMCs performed worse than controls on free recall on the first trial, total free recall, and total delayed recall on the FCSRT. Additionally, older people with SMCs had increased density power in theta, as well as a loss of central alpha reactivity to EO. However, we did not find differences in young people with SMCs, compared to controls, in the power spectral of the bands or in EEG reactivity. In addition, in older people with SMCs in the EO condition, higher theta was associated with better verbal memory.

As the neuropsychological assessment revealed, older people with SMCs obtained lower scores on free recall on the first trial and on total recall on the FCSRT and DS-Forward, compared to the control group, but no other significant differences were observed on any of the cognitive measures. Likewise, young people with SMCs also obtained lower scores on free recall on the first trial, total free recall, and total delayed recall on the FCSRT, compared to the control group. This result agrees with previous studies that have either reported a weak association (López-Sanz et al., 2016) or no association (Lazarou et al., 2018; Park et al., 2019) between SMCs and objective cognitive performance. Specifically,

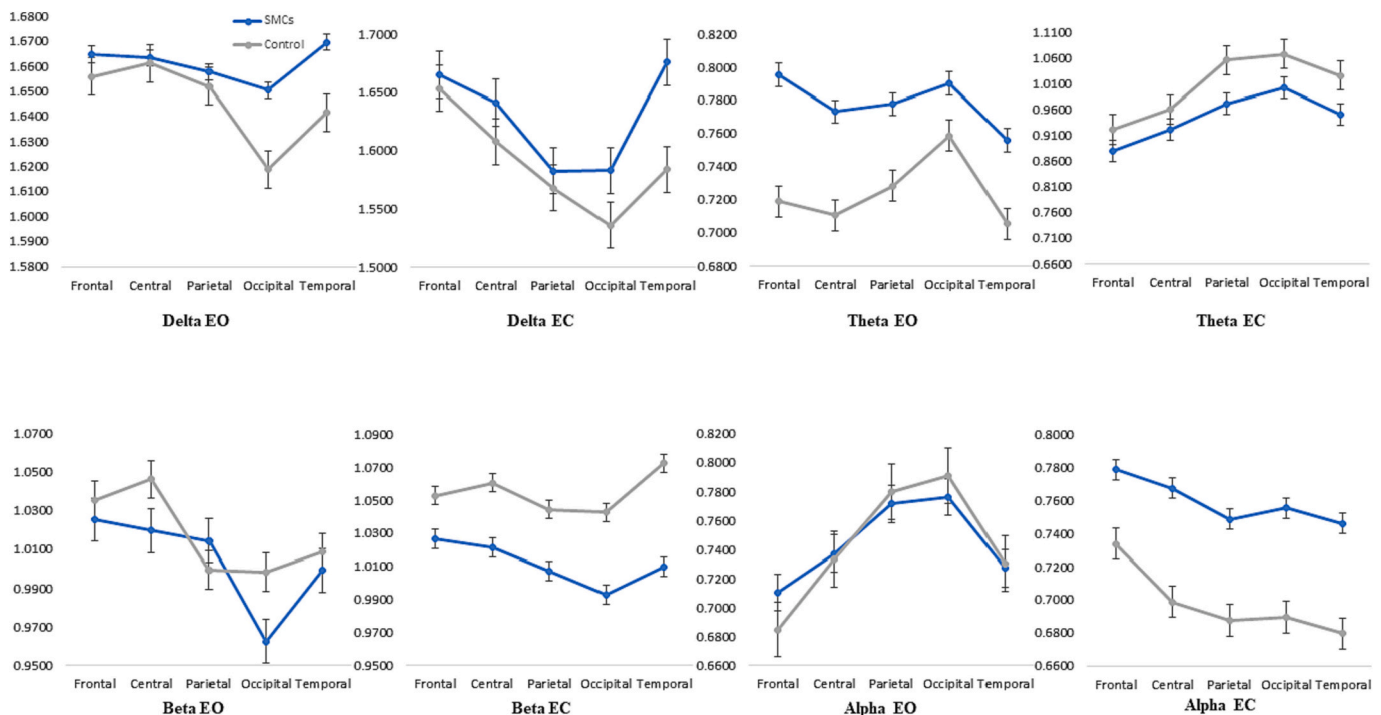


Fig. 1. Means values and standard deviations of EEG spectral power analysis relative to the interaction effects among three factors: older groups (SMCs: subjective memory complaints and control), frequency bands (delta, theta, beta, alpha), and condition (EO: eyes open, EC: eyes close).

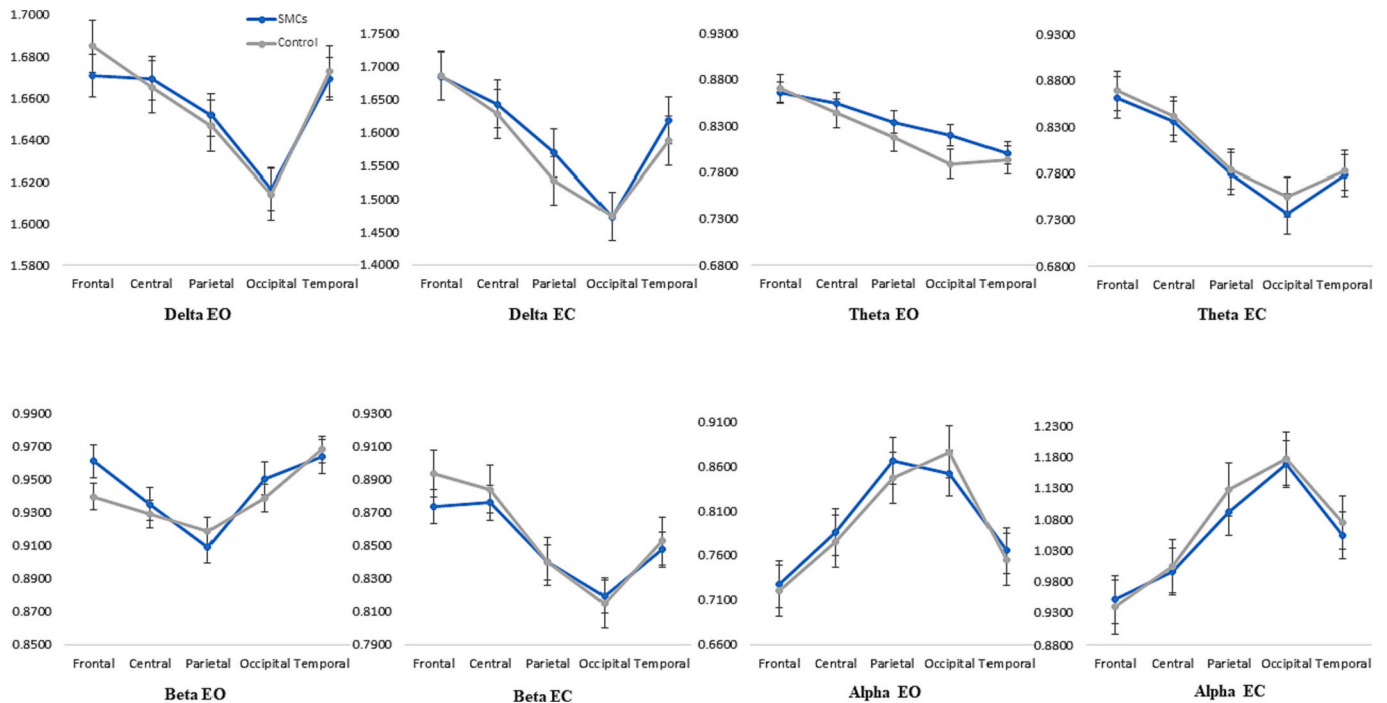


Fig. 2. Means values and standard deviations of EEG spectral power analysis relative to the interaction effects among three factors: young groups (SMCs: subjective memory complaints and control), frequency bands (delta, theta, beta, alpha) and condition (EO: eyes open, EC: eyes close).

Table 2

Correlations between theta power and alpha reactivity and neuropsychological measures for subjective memory complaint and control groups.

Older group	SMCs			Control		
	Verbal memory	Executive function	Attention	Verbal memory	Executive Function	Attention
Eyes-open theta						
Frontal	<i>r = 0.302; p = .105</i>	<i>r = 0.057; p = .765</i>	<i>r = -0.095; p = .617</i>	<i>r = 0.077; p = .649</i>	<i>r = -0.034; p = .841</i>	<i>r = -0.039; p = .821</i>
Central	<i>r = 0.365; p = .047</i>	<i>r = -0.021; p = .911</i>	<i>r = -0.188; p = .319</i>	<i>r = 0.114; p = .502</i>	<i>r = -0.045; p = .792</i>	<i>r = -0.096; p = .570</i>
Parietal	<i>r = 0.358; p = .052</i>	<i>r = 0.118; p = .534</i>	<i>r = -0.200; p = .290</i>	<i>r = 0.009; p = .959</i>	<i>r = -0.096; p = .570</i>	<i>r = -0.163; p = .334</i>
Occipital	<i>r = 0.128; p = .502</i>	<i>r = 0.062; p = .747</i>	<i>r = -0.257; p = .171</i>	<i>r = -0.041; p = .811</i>	<i>r = 0.003; p = .985</i>	<i>r = 0.057; p = .736</i>
Temporal	<i>r = 0.338; p = .068</i>	<i>r = 0.102; p = .590</i>	<i>r = -0.207; p = .273</i>	<i>r = 0.077; p = .651</i>	<i>r = -0.082; p = .631</i>	<i>r = -0.101; p = .552</i>
Alpha reactivity						
Alpha central	<i>r = -0.059; p = .745</i>	<i>r = 0.099; p = .585</i>	<i>r = -0.004; p = .985</i>	<i>r = 0.210; p = .210</i>	<i>r = 0.207; p = .226</i>	<i>r = 0.069; p = .690</i>

Note: Significant correlations are displayed in bold. In correlation analyses we represent all correlations in italic and significant correlations in bold with italic. Abbreviations: SMCs, subjective memory complaints; Control, no subjective memory complaints.

López et al. (2016) showed that SMCs scored lower on immediate and delayed recall than controls; however, on most of the tests employed that contained working memory, language, executive functions, and praxis, SMCs performed equal to controls. Despite this, several studies found that, although SMCs are inconsistently associated with objective measures of cognitive functions, these complaints may predict the risk of future cognitive decline (Glodzik-Sobanska et al., 2007; Mitchell et al., 2014; Reid and MacLulich, 2006). This statement is supported by a prospective longitudinal study that reported that approximately 2.3 % and 6.6 % of older people with SMCs, respectively, will progress to dementia and MCI per year compared to 1 % in people without SMCs (Mitchell et al., 2014). Moreover, several studies have observed neurophysiological changes in people with SMCs, such as smaller left hippocampal volume (Flier et al., 2004), atrophy of the anterior cingulate cortex, medial prefrontal cortex, cuneus, precuneus, and precentral gyrus (Hafkemeijer et al., 2013), and reduced volume of the hippocampus bilaterally, the bilateral entorhinal cortex, and the right amygdala, compared to the control group (Striepens et al., 2010).

In keeping with our first hypothesis, previous studies have shown

that an increase in theta power is correlated with different degrees of hippocampal atrophy (Babiloni et al., 2012; Moretti et al., 2007), which is one of the earliest and most sensitive EEG changes in the neuropathology of MCI and AD (Babiloni et al., 2012; Moretti et al., 2007; Roh et al., 2011). From a functional point of view, the increase in the theta band power is a sign of cortical activation, in particular, an increase in the activity of the hippocampal-medial prefrontal pathways (Moretti et al., 2007). According to these authors, when hippocampal atrophy reaches a discrete feature, compensatory theta activity begins. Our results are in agreement with previous studies showing an increment of theta power in older people with SMCs (Alexander et al., 2006; Gouw et al., 2017; Prichep et al., 1994). But what is the physiological meaning of these changes in theta density power in subjects with SMCs? An important candidate to explain these changes is the cholinergic deficit, given that previous studies have shown that acetylcholine and the basal forebrain system maintain desynchronized EEG activity (Jeong, 2004). Thus, a loss of cholinergic innervation of the neocortex may lead to an increase in theta power (Jeong, 2004; Roh et al., 2011). The critical role of cholinergic deficit is also supported by EEG studies using

scopolamine, which is a nonselective antagonist of muscarine receptors that blocks stimulation of postsynaptic receptors. After administration of scopolamine, an increase in delta and theta power and a decrease in alpha and beta power are observed in healthy subjects (Ebert et al., 2001). Alternatively, it has been suggested that thalamocortical circuitry underpins the generation and modulation of theta rhythms. Analogous mechanism in the thalamocortical circuitry is associated with alpha rhythms. In this regard, Bhattacharya et al. (2011) used computational models of thalamocortical circuitry to understand the underlying neural behavior associated with EEG changes in the power spectra within the theta and lower and upper alpha bands in AD. An increase in inhibitory feedback from the thalamic reticular neurons population to the thalamocortical relay population results in an increase in power within the theta band, and a decrease of the power within the alpha band, leading to an overall decrease in the dominant frequency of the power spectra. Therefore, the thalamic reticular neurons appear to play a crucial role in mediating the behavioral traits of the model output, which fits biological studies that show an important role of inhibitory feedback of the thalamic reticular neurons in shaping the oscillatory behavior of the circuit thalamus-cortico-thalamus. Thus, the afferent and efferent pathways of the thalamic reticular nucleus may provide crucial clues for a better understanding of the EEG slowing seen in AD (Bhattacharya et al., 2011). Although this model is plausible, it is limited by the lack of inclusion of cortical and cholinergic inputs, both of which are believed to be important.

Regarding the EEG reactivity hypothesis, older people with SMCs also showed a loss of EEG reactivity at central alpha power in EO. Previous studies carried out in this population have produced contradictory results. On the one hand, Alexander et al. (2006), using global phase synchrony, found no significant differences in SMCs compared to their matched controls. On the other hand, Pijnenburg et al. (2008), using synchronization likelihood, found that people with SMCs showed a loss of reactivity. An explanation for our findings for the central alpha could be an incipient neurodegenerative process that first affects neural synchronization in this frequency band. Alpha activity originates from thalamo-cortical and cortico-cortical interaction, and it is modulated by neurotransmitter acetylcholine (Goldman et al., 2002). Hence, this loss of reactivity may be associated with the aforementioned cholinergic dysfunction. Moreover, cholinergic dysfunction has been related to changes observed in alpha activity, but also to alterations in attention and executive functioning in people with neurodegenerative cognitive impairment (Lejko et al., 2020).

Regarding the relationship between resting EEG and cognitive function, our results showed that, in older people with SMCs, increased central theta spectral power was correlated with better performance on verbal memory. Previous EEG studies carried out with this population have also shown an increase in theta power and better memory performance, including working and verbal memory (Alexander et al., 2006). It has been well documented that during the encoding, retention, and retrieval intervals, theta power increases (Klimesch et al., 2008), and that it is involved in the transfer of information between the working memory and long-term memory systems (Sauseng et al., 2002). In line with these findings, Buzsáki (2005) proposed a model of temporal encoding, given that theta is critical to establishing temporal associations between stimuli, which can occur during navigation or when experiencing arbitrary stimulus sequences, such as words in a free recall task. In a recent review, Herweg et al. (2020) determined that successful memory is associated with increased narrowband theta oscillations, and that theta oscillations specifically support associative memory. Therefore, as previously discussed, older people with SMCs exhibit some EEG changes, such as an increase in theta, that further correlate with verbal memory. This suggests that cholinergic innervation or abnormal intrathalamic activity may interfere with efficient cognitive processing. Note that older people with SMCs also performed worse than their matched controls on some of the verbal memory subtests, reinforcing the findings indicating that physiological changes are related to deficits in

performance on some cognitive tasks.

Although SMCs are also frequent in young people, we were not able to demonstrate any differences between young people with SMCs and controls in the power spectral or EEG reactivity. The absence of EEG differences between groups might indicate that the electrical activity of the brain is relatively preserved.

In the interpretation of these findings, it is important to consider that the present study follows a cross-sectional design, which limits the extent to which we can identify power spectral changes in longitudinal cognitive decline in older people. In addition, it should be noted that we made an effort to reduce the number of variables and clustered them into three neuropsychological domains. Despite this limitation, this study benefits from a complete assessment of neurocognitive function that objectively establishes the absence of deterioration in SMCs.

5. Conclusion

In general, the present results confirm previous evidence showing that older people with SMCs are characterized by distinct power resting state EEG rhythms, especially at increased theta power, and a slight loss of EEG reactivity to EO. These findings suggest that neurophysiological markers of brain dysfunction may identify cognitive decline and changes before they are observed in a neuropsychological assessment. Furthermore, these changes could also help us to better understand the neurophysiological mechanisms affected by neurodegeneration.

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Data availability

Data will be made available on request.

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