VNIVERSITAT DE VALÈNCIA

University of Valencia

Department of Psychobiology

PhD in NEUROSCIENCE (3142)

Neurophysiological markers of subjective memory complaints in healthy people

Marcadores neurofisiológicos de las quejas subjetivas de memoria en personas sanas

PhD Thesis

Presented by:
Joana Vanesa Perez

Promotor:
Dra. Alicia Salvador Fernández-Montejo
Dra. Vanesa Hidalgo Calvo

Valencia, July 2022

Neurophysiological markers of subjective memory complaints in healthy people

Marcadores neurofisiológicos de las quejas subjetivas de memoria en personas sanas

Joana Vanesa Perez

ACKNOWLEDGEMENTS/AGRADECIMIENTOS

Al finalizar un trabajo arduo y lleno de dificultades como una tesis doctoral es necesario agradecer a las personas y a la institución que ha posibilitado que este trabajo se desarrolle y finalice. Este trabajo lleno de aprendizaje y constate crecimiento fue posible gracias al apoyo de muchas personas, a todas ellas ¡gracias!.

Debo agradecer, en primer lugar, a la profesora Alicia Salvador por aceptarme para realizar esta tesis en su laboratorio y bajo su dirección. También debo agradecer a Vanesa Hidalgo, ambas han guiado este proceso acompañando mis ideas y han enriquecido este trabajo con sus aportes. Su apoyo, confianza y generosidad para compartir sus experiencias y conocimientos han sido de gran ayuda no sólo para el desarrollo de esta tesis sino también en mi formación como investigadora.

Gracias también a todas las personas que forman este grupo de investigación (Teresa, Inés, Lorena, Mario, Ruth, Mariola, Isabel, Matías y Valerie). Compartir tiempo, experiencias, preocupaciones y alegrías cada día y tras cada artículo publicado ha hecho que este camino sea más fácil de transitar. Gracias porque con muchos, además de ser compañeros/as en este proceso, hemos forjado una bonita amistad.

También quiero agradecer al profesor Fernando Barbosa por su amabilidad, disponibilidad y colaboración durante mi estancia de investigación en su laboratorio. También a todos los que forman parte de su grupo de investigación, sin duda su pasión por la psicobiología es contagioso y un especial agradecimiento a Tiago Paiva por su asesoramiento en los análisis y su compañerismo.

También agradecer al Ministerio de Educación y Ciencia de España por la subvención que ha posibilitado la investigación plasmada en esta tesis y a la beca Iberoamérica, Santander Investigación la cual me permitió realizar la estancia de investigación.

Por último, agradecer a las personas más importantes para mí. En primer lugar, a mi compañero de vida, Ivan, por su apoyo y motivación constante, por acompañar todas mis elecciones. Sin duda, este camino se ha hecho más sencillo gracias a su compañía.

También a mi familia. A pesar de las distancias, mis padres y mis hermanas han sido una compañía constante y un motor que me impulsó a continuar y finalizar este proceso. También agradecer a mis amigas Ana, Lorena, Yamila y Gisela que han sido una compañía y apoyo en la distancia.

THESIS OUTLINE

Subjective memory complaints (SMCs) are very common in older people, but they also are reported by young people. SMCs are of increasing interest mainly because they make it possible to identify individuals with a pronounced risk of future cognitive impairment, even in the presence of normal baseline objective cognition. Therefore, it is important to investigate reliable early biomarkers for the detection and planning of treatments for people at risk of cognitive impairment and dementia.

Among these biomarkers, electrophysiological measures derived from electroencephalogram (EEG) are a method of interest. EEG is an affordable technique, easy to perform, and widely used from a neuropsychological approach to dementia-related disorders (Babiloni et al., 2016). Many issues about SMCs are still unclear, and therefore it is necessary to increase the knowledge about neurophysiological markers that could contribute to explaining them. Hence, this thesis aims to address neurophysiological markers related to SMCs. In this regard, an insight into facial emotion processing in both young and older people is provided, as well as the main event related potentials (ERPs) used to temporally characterise emotional processing in the human brain together with behavioural measures of reaction time (RT) and accuracy. In addition, resting state electroencephalographic rhythms at different frequency bands, EEG reactivity, or alpha peak parameters are under-explored neurophysiological mechanisms that could contribute to understanding SMCs in young and older people.

Chapter one presents a general introduction to the studies included in this thesis. First, the current literature on the definition and prevalence of SMCs and their relationship with cognitive function is presented. Likewise, EEG is also described as a tool to investigate neural changes in SMCs. In addition, facial emotion processing and the main ERPs used are described

because some studies have shown a deficit in facial emotion processing in mild cognitive impairment (MCI) (for review, see: McCade et al., 2011) and Alzheimer's disease (AD) (for review, see: Elferink et al., 2015). Finally, power spectral, EEG reactivity, and alpha peak parameters are also presented in Chapter one.

Chapter two includes the main objectives and hypotheses of this thesis.

Chapter three describes the first study. This study explores whether facial emotion processing is different in young people with and without SMCs who were exposed to positive, negative, and neutral faces. To do so, the two main processing components (N170 and LPP) usually studied in this context were employed, and behavioural data (RT and accuracy) were included. In addition, possible sex-related differences in young people with and without SMCs were studied.

Chapter four explains the second study, which determines whether there are differences in the neuronal correlates and behavioral measures of facial emotion processing between older people with and without SMCs, as well as a possible association between ERPs measures and executive performance (EF), as proposed by some authors (Pietschnig et al., 2015; Sarabia-Cobo et al., 2015; Schefter et al., 2012; Teng et al., 2007; Wang et al., 2015).

Chapter five includes the third study. This study presents the analyses of the spectral power of EEG resting state frequency bands and EEG reactivity in older and young people with and without SMCs. In addition, we explore whether there is a correlation between the region- and frequency-specific spectral powers and neuropsychological measures.

Chapter six describes the fourth study. This study investigates alpha peak parameters, such as alpha peak frecuency (APF) and amplitude, in SMCs and control people. In addition, in this chapter, we investigate whether these parameters would not only differentiate SMCs and

control, but also young and older people, as well as men and women. Finally, the association between cognitive reserve (CR) and alpha peak parameters is explored.

Chapter seven contains a general discussion and the main findings of the above-mentioned chapters, the limitations and strengths of this thesis, and directions for future research. Chapter eight presents the main conclusions of this thesis. Finally, this thesis ends with Chapter nine, which includes a general summary in Spanish, as well as the references and the funding obtained.

ABBREVIATIONS

AD = Alzheimer's disease

APF = Alpha Peak Frequency

AWMA = Automated Working Memory Assessment

BDI-II = Beck Depression Inventory-II

BMI = Body Mass Index

CR = Cognitive Reserve

DS-Backward = Digit Span Backward

DS-Forward = Digit Span Forward

EC = Eyes Closed

EEG = Electroencephalogram

EF =Executive Function

EO = Eyes Open

ERPs = Event-related Potentials

FCSRT = Free and Cued Selective Reminding Test

FFT = Fast Fourier Transform

IAPS = International Affective Picture System

KDEF = Karolinska Direct Emotional Faces

LPP = Late Positive Potential

MCI = Mild Cognitive Impairment

MRI = Magnetic Resonance Imaging

MFE-30 = Memory Failures of Everyday

noSMCs = No subjective Memory Complaints

PET = Positron Emission Tomography

ROI= Regions of Interest

RT =Reaction Time

SCD = Subjective Cognitive Decline

SCD-I = Subjective Cognitive Decline-initiative

SES = Subjective Socioeconomic Status

SMCs = Subjective Memory Complaints

TMT = Trail Making Test

TABLE OF CONTENTS

CHAPTER 1.
GENERAL INTRODUCTION

1.1 SUBJECTIVE MEMORY COMPLAINTS: DEFINITION AND PREVALENCE

With the aging of the population, which is expected to double by 2050, it is important to further understand the neurophysiological changes that occur during aging. This is relevant both in the context of pathological aging and what is considered normal or healthy. Specifically, a large proportion of older people are affected by age-related decline (Juan & Adlard, 2019; World Health Organization [WHO], 2018). In this context, concerns about cognitive changes are becoming a topic of interest because the number of people with this concern who seek medical help is growing (Jessen, 2020). These changes in cognitive capacity are reflected in the subjective perception of the people in question. Since 1980, the association between subjective memory deficits without objective evidence of memory deficits in clinical interviews or social situations and the future risk of cognitive decline has been addressed (Reisberg et al., 1982). The concept of subjective memory complaints (SMCs) can be defined as subjective awareness of memory loss in the absence of any organic or identifiable condition in neuropsychological examinations (Schmand et al., 1996). In previous studies, this concept has been referred to as subjective cognitive impairment, subjective memory decline, subjective memory impairment, and memory complaints (Abdulrab & Heun, 2008; Ginó et al., 2010; Rowell et al., 2015).

With the aim of facilitating the development of a common concept and terminology, in 2012, an international working group known as the Subjective Cognitive Decline-Initiative (SCD-I) was formed that included researchers and clinicians on Alzheimer Disease (AD) from many countries. This working group proposed the name “Subjective Cognitive Decline” (SCD; Jessen et al., 2014), which included two features:

(1) a self-experienced persistent decline in cognitive capacity, compared with a previously normal cognitive status. “Cognitive” refers to any cognitive domain, and it is not limited to memory decline. “Decline” reflects the subjectively experienced progressive nature of cognitive deterioration.

(2) normal performance on standardised cognitive tests used to classify Mild Cognitive Impairment (MCI), adjusted for age, sex, and education.

Despite this, SMCs are the primary feature of SCD (Sohrabi et al., 2018), and they are referred to the most by those who consult their doctor. SMCs are reported frequently by older adults who often complain about changes or a decline in their memory (Jacob et al., 2019; Meyer et al., 2017; Montejo et al., 2019; Vlachos et al., 2019). However, SMCs are also communicated by young people, although less frequently (Ginó et al., 2010; Rowell et al., 2015; Sohrabi et al., 2018; Loprinzi, 2019; Mendes et al., 2008).

Population-based studies suggest that a high percentage of older people report some form of perceived decline in cognitive functioning, with the percentage ranging from 10.5% to 76% depending on age and other characteristics. A study carried out in Madrid showed that almost 32.4% of older adults reported SMCs (Montejo et al., 2011). Another study conducted on older adults from the United Kingdom showed that the prevalence of SMCs ranges from 10.5% to 15.6% (Begum et al., 2013). Vlachos et al. (2019), in the Greek population, found that 76.6% have memory complaints, and Schütz et al. (2020), in the German population, observed a prevalence of 65.9 % in people over 55 years of age.

Even in the youngest age group, prevalence of SMCs varies but is relatively high, ranging from 5.5% to 30%. In a German population-based sample of young people in the age range from 18 to 34 years, prevalence of SMCs was already 30.1% (Schütz et al., 2020). However, in another study conducted in the United Kingdom, the estimated prevalence ranged between 5.5% and 7.9% in people up to 34 years old (Begum et al., 2013).

The reasons for these large variations are diverse: studies were conducted in different situations, for example, community-based cohort, primary care, and clinic settings. In addition, different methods are employed to assess SMCs: some researchers use a single question, set of

questions or criteria, questionnaires, or subscales (Abdulrab & Heun, 2008). Thus, although these different approaches to measuring and classifying SMCs may correlate one with another, they are not identical; hence, findings of the different investigations cannot be directly compared.

Likewise, the prevalence between sexes also varies and depends largely on the methods applied or selection biases because men tend to have a lower participation rate in studies (Holmen et al., 2013). Only a few studies have reported sex differences in SMCs, with inconsistent results. One of them found a higher prevalence in women (Genziani et al., 2012), whereas in another study, men reported more memory problems than women (Holmen et al., 2013).

1.2 SUBJECTIVE MEMORY COMPLAINTS AND OBJECTIVE COGNITIVE FUNCTION

An important contribution to understanding memory complaints is to determine to what extent this heterogeneous phenomenon is related to objective performance on cognitive tests. Studies investigating the association between memory complaints and memory performance have largely yielded inconsistent results in healthy older people. In some studies, SMCs have been related to worse objective neuropsychological performance (Burmester et al., 2016; Brailean et al., 2019; Cespón et al., 2018; Kim et al., 2017; Vaskivuo et al., 2018). However, other studies have demonstrated a weak relationship or no relationship between subjective and objective memory performance (Lazarou et al., 2018; Lee et al., 2017; Park et al., 2019; Rowell et al., 2015; Zlatar et al., 2018). Similar discrepancies have been found in young people with SMCs. On the one hand, some studies have related SMCs in young people to poorer performance on cognitive tests (MolinaRodríguez et al., 2018; Ruiz-Sanchez de León et al.,

2010; Schweizer et al., 2017). On the other hand, no such association has been found in other studies (Ginó et al., 2008; Montenegro et al., 2013).

There could be various reasons for these inconsistencies. One would involve methodological limitations, such as unvalidated measures of complaints and failure to assess confounding variables of depression and/or personality (Jacob et al., 2019). Another reason may be that, even though memory declines over time, the decline may be too subtle to be assessed with standard neuropsychological tests (Crumley et al., 2014). In addition, these inconsistencies could also be explained by cognitive reserve (CR). The CR construct is used to explain why two people may have different clinical manifestations of the same disease (Stern, 2012), and it can be studied by measuring latent variables related to life experience, such as education, working activity, and leisure activities (Jones et al., 2011). The protective effect of CR has been studied in healthy people (Pettigrew & Soldan, 2019), people with SMCs (Lojo-Seoane et al., 2018), and people with MCI (Constantinidou et al., 2014), and some studies have found that higher levels of CR are associated with a reduced risk of progressing towards dementia. Contradictory results led to the need to investigate the neurophysiological basis of SMCs in order to obtain a better understanding of SMCs and their possible correlation with changes in brain functionality. In this vein, facial emotion processing is an important topic in neurophysiological research, and it is also a cognitive function that is commonly affected in people with neurodegenerative diseases (Lazarou et al., 2018).

1.3 SUBJECTIVE MEMORY COMPLAINTS AND FACIAL EMOTION PROCESSING

Emotions are one of the most basic psychophysiological reactions people have, and they are perceived mainly through facial expressions. Facial expressions inform about how

people feel and their action tendency (Wang et al., 2015), and they are a key channel for social communication (Schindler & Bublatzky, 2020). Facial emotion processing is crucial to interpersonal relationships and the prediction of prosocial or aggressive behavior. In addition, it is considered an important prerequisite for better quality of life (Hinojosa et al., 2015). Deficits in facial emotional processing have been extensively studied in neurodegenerative diseases such as AD (see review: Elferink et al., 2015) and prodromal phase of dementia such as MCI (see review: Bora & Yener, 2017). Some findings suggest that subtle deficits in the processing of emotional expression appear already in SMCs (Lazarou et al., 2018; Pietschnig et al., 2015).

Emotion processing has been shown to rely on a complex affective system, including the amygdala, insula, ventral striatum, and ventral regions of the anterior cingulate gyrus and prefrontal cortex (Phillips et al., 2003), inferior occipital temporal cortex, fusiform gyrus (Eimer & Holmes, 2007), basal ganglia, and right parietal cortices (Adolphs, 2002). Using neuroimaging techniques, some researchers have demonstrated that some brain regions of this system are already susceptible to atrophy in SMCs (Hafkemeijer et al., 2013; Van Flier et al., 2004).

Cognitive factors also influence facial emotional processing and, therefore, should be considered. Attention, for example, is an essential cognitive resource in facial emotional processing. From an evolutionary perspective, it has allowed us to detect emotional facial information that indicates possible signs of potential harm in the environment (Calvo & Beltrán, 2013). In this regard, two mechanisms involved in the orientation of attention and processing resources have been described, one of them controlled and the other rather automatic (Schindler & Bublatzky, 2020). On the one hand, attentional focus can be allocated

by voluntary and controlled processes that depend on higher-order processing areas (Petersen & Posner, 2012). This top-down control of attention is initiated, for example, by spatial cues or task instructions (Polich, 2007). On the other hand, attentional focus can also be driven from the bottom up, that is, quite automatically by the inherent value of biological or emotional stimuli. Importantly, top-down and bottom-up emotional salience can be considered interconnected phenomena (Schindler & Bublatzky, 2020).

Executive function (EF) is a high-order cognitive domain related to complex problem-solving skills, information retrieval, organizational strategies and concept formation, perceptual selection, detection and resolution of conflict, and maintenance of contextual information, processes that are involved in making judgments about emotional expressions (Cristofori et al., 2019; Pessoa, 2009). Traditionally, EF has been associated with frontal lobe functioning, although recent evidence has shown that posterior and subcortical regions also play a crucial role in EF, especially in the integration of sensory information and emotion (Cristofori et al., 2019).

As noted above, certain cerebral structures and cognitive domains are clearly related to the ability to process emotional facial expressions. This ability can be examined by presenting photographs of faces expressing different emotional valences. In this photographic format, the Karolinska Direct Emotional Faces (KDEF; Lundqvist et al., 1998) has been frequently utilized, which classifies emotional stimuli according to valence (negative, positive, and neutral). At the neural level, facial emotion processing can be assessed by electroencephalogram (EEG), which is an excellent tool for examining the temporal dynamics of emotional face processing (Olofsson et al., 2008).

1.4 ELECTROENCEPHALOGRAPHY

The EEG has been widely used by the scientific community because it is a relatively affordable technique that allows a direct, non-invasive, and real-time measurement of brain neuronal activity. In this vein, EEG is tolerated well by people of all ages from premature neonates to the elderly (Biasiucci et al., 2019). EEG is characterized by low spatial resolution compared to structural magnetic resonance imaging (MRI) and positron emission tomography (PET), but EEG provides high temporal resolution (Rossini & Forno, 2004). It should be noted that the high temporal resolution of EEG is essential in the study of event-related potentials (ERPs) and activity at different frequency bands (Babiloni et al., 2020a; Luck, 2014).

EEG measures the brain's electric field resulting from ionic currents generated by biochemical processes at the cellular level. The primary source of the EEG signal arises from synchronized synaptic activity in populations of cortical neurons (pyramidal cells organized by cortical columns; Holmes & Khazipov, 2007). When a group of neurons discharges simultaneously, a movement of ions is produced, generating an electric field. The postsynaptic potentials are responsible for the signal recorded in the EEG. The postsynaptic potentials result from relatively slower currents after neurotransmitter release at the axon's terminal boutons. The anatomical features of individual pyramidal neurons and their orderly arrangement in columns in most cortical areas facilitate EEG measurement (Biasiucci et al., 2019). These measurements are made as follows: an excitatory postsynaptic potential of postsynaptic neurons creates an extracellular voltage near neural dendrites that is more negative than in other parts of the neuron. This situation is known as a dipole: a region of positive charge separated from a region of negative charge by some distance. The region of positive charge is called the source, whereas the region of negative charge is called the sink (Jackson & Bolger, 2014). In the soma, there will be an intracellular current sink and an extracellular current source. These source-sink configurations are the main source of potentials measured by EEG. To be

measurable on the surface of the scalp, neuronal populations must be active simultaneously. This allows the summation of currents that are then conducted in an isotropic manner, regardless of their frequency spectra, throughout the volume of the brain, crossing all the protective mechanisms of the brain to the EEG electrodes (Biasiucci et al., 2019; Luck & Kappenman, 2011).

Electrodes composed of conductive materials placed on the scalp detect the sum of positive and negative charges in their area. Because electrodes detect the sum of charges in their area, the dipoles from multiple neurons in a region will be added together. However, because electrodes will measure the sum of both the positive and negative ends of dipoles in the brain, to produce a measurable (i.e., nonzero) signal, neurons must be arranged in a parallel manner and synchronously active (Jackson & Bolger, 2014).

In order to be measured with an electrode outside the head, the electrical signal must travel from the brain, through the cerebrospinal fluid, the dura mater, the skull, the muscles, fat, skin, and, finally, to the electrode. When the signal conducted reaches the edge of the volume through which it travels, its conduction can no longer occur because the ions cannot abandon the volume. Between volumes, capacitance becomes responsible for the propagation of the signal. A capacitor consists of two groups of charges separated by an insulating layer. If there is an insulating layer, a charge difference can build up where negative ions push against one side of the membrane and positive ions accumulate on the other side. The amount of charge that accumulates on the other side is determined by the properties of the insulating materials between the charge groups, the size of the charged group, and the distance between the charge group and the insulating layer. The sequence of layers from the brain to the dura, the skull layers, the scalp layers, the electrode gel, and the electrodes forms a series of conductive volumes separated by insulating layers, like a stack of capacitors (Jackson & Bolger, 2014).

As noted above, inside the brain, the EEG signal is transmitted by volume conduction, but once the signal reaches the skull, it can no longer be carried by ions because the ions do not pass through the skull. Although cerebrospinal fluid and other ion-filled substances in the brain are good conductors, they are separated from the electrode by layers of poor conductors, such as skin cells or hair. Thus, it usually requires an electrolytic interface (i.e., electrolytic gel). The electrolytic gel, which is highly conductive, will saturate the space under an electrode, filling the pockets of air between the hairs, thus generating a conductive path from the scalp to the electrode (Usakli, 2010; Jackson & Bolger, 2014). Figure 1 represents the transmission of the signal from the brain to the electrode.

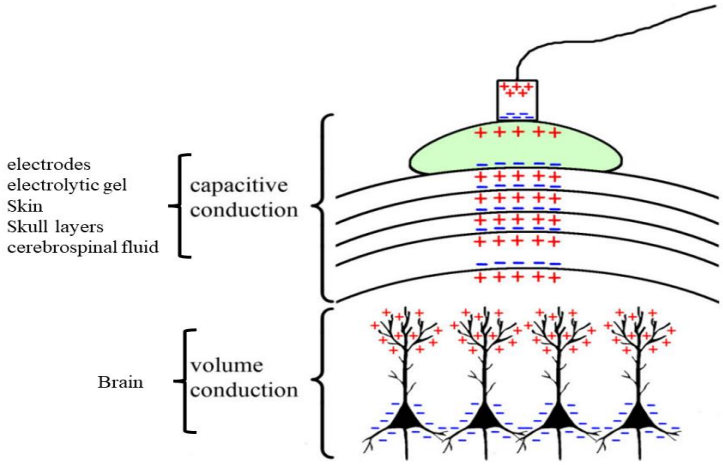


Figure 1.1. Transmission of the signal from the brain to the electrode. The capacitor is stacked with electrolytic gel, showing the neural signal transmitting through the different protective barriers of the brain (i.e., cerebrospinal fluid, skull layers, skin), and electrolytic gel to reach electrodes. Because electrolytic gel is a conductor, the signal reaches the electrode with less attenuation. Adapted from Jackson & Bolger, 2014.

The EEG system measures electrical activity that arises from the brain as well as external sources (i.e., lights, computer monitor, etc). This external noise can be resolved by two methods: passive shielding and active electrodes. A passive shield is essentially a piece of conductive metal that surrounds the region to be protected and cancels or deflects electromagnetic radiation (Dugdale, 1993). Active electrode systems place an amplifier as

close to the electrode as possible. Amplifying the signal before running it over an unshielded cable means that even if noise is introduced while the signal travels to the main amplifier, the signal-to-noise ratio is still quite large. The signal-to-noise is a measure of the amount of signal that the system measures compared to the amount of noise; a larger signal reflects better quality (Jackson & Bolger, 2014).

The functions of an amplifier in an EEG system are, on the one hand, to maximize the signal-to-noise ratio of the measured voltage, and on the other hand, increase the size of a signal beyond the size of the noise that can be introduced into circuit elements. For example, a signal that is measured at the scalp must travel through a cable to reach the acquisition computer. Noise can be introduced at this point of measurement. If the signal is amplified before noise is introduced, the impact on the signal-to-noise will be reduced (Jackson & Bolger, 2014). Innovations in amplifier design have allowed for faster sampling rates and increased numbers of simultaneously recorded channels (Biasiucci et al., 2019). In addition, it is important to highlight the input impedance of an amplifier, which is vital for EEG collection. The input impedance determines how well the amplifier can tolerate a poor connection to the scalp (Self, 2009).

EEG technology opened up new possibilities to explore human emotion, cognition, and actions as they occur. As noted previously, ERPs enable the assessment of these neural responses with millisecond temporal resolution (Olofsson et al., 2008).

1.5 EVENT RELATED POTENTIALS

ERPs components appear on the scalp as a series of positive and negative peaks that differ in polarity, amplitude, and duration over time and reflect the sensory, cognitive,

affective, and motor processes elicited by a stimulus (Luck & Kappenman, 2011). ERPs are measured by assessing their amplitude (size) and latency (timing). Amplitude (pV) is defined as the voltage difference between a prestimulus baseline and the largest positive-going peak of the ERP's waveform within a latency window. Latency (ms) is defined as the time from stimulus onset to the point of maximum positive amplitude within the latency window (Luck et al., 2000).

Emotional information processing can be assessed with ERPs. Thus, brain potentials recorded from the scalp are a valid means of characterizing emotional and temporal processing in the human brain (Olofsson et al., 2008). Compared to neutral stimuli, emotional stimuli modulate a broad range of ERPs, beginning with early perceptual processing and continuing to later stages that involve elaborative processing (Hajcak & Foti, 2020).

1.5.1 N170 Component

Many emotional ERPs modulations for face stimuli have been reported in the 100-200 ms range. The N170 is a negative component elicited at 150-170 ms. This component is more prominent over the visual cortex (occipitotemporal sites) and shows a more consistent lateralization of the right hemisphere (Luo et al., 2010; Rossion, 2014). In addition, this time window precedes potential saccadic eye movements, which take 200 ms to initiate (Rossion, 2014). N170 has been proposed as a correlate of the interpretation of a visual stimulus such as a face, and it depends on our knowledge and experience of what a face is, incorporating both bottom-up and top-down processes. For instance, objects that can be consciously interpreted as face-like, such as character combinations known as emoticons (Churches et al., 2014) or Arcimboldo paintings (because they are composed of non-face objects but have a global face configuration) enhance the N170 (Caharel et al., 2013). In the same vein, N170 is not enhanced

by other types of stimuli (i.e., by furniture, cars, hand gestures; Zhao et al., 2019) or an inverted emoticon (i.e., not interpreted as a face; Churches, 2014).

Researchers have tried to localise the source of the N170 using a variety of algorithms (Rossion & Jacques, 2008). However, source localisation is difficult in face processing because this function is widely disseminated across the ventral occipitotemporal cortex (Rossion, 2014). Despite this, a study combining functional MRI and ERPs suggested that the face selective N170 component emanates from the temporal lobe (i.e., fusiforme gyrus) and temporal sulcus (Sadeh et al., 2010).

Moreover, several studies have compared the effects of N170 elicited by emotional and neutral facial expressions, with inconsistent results. Early studies failed to find any effect of facial expression on N170 (Eimer, 2000; Holmes et al., 2005). These results support the theory of this component as a correlate of the structural encoding face (Eimer & Holmes, 2007). Nevertheless, years later, a meta-analysis validated robust emotion effects at the level of the N170 component (Hinojosa et al., 2015), which suggests that N170 is sensitive to face expression and does not strictly reflect an encapsulate encoding of the structural representation of faces. Some more recent experimental studies also demonstrate that N170 can be modulated by the emotional valence (Qiu et al., 2017).

Emotional modulations have consistently been shown by latent components such as P300 and late positive potential (LPP). Both components reflect waveform differences between emotional valences compared to neutral faces.

1.5.2 P300 component

The P300 is a widely studied component and one of the first reported. Its discovery was due to the convergence between the increased technological capacity for signal averaging

applied to human neuroelectric measurements and the impact of information theory on psychological research (Sutton et al., 1979). The P300 component produces a large positive-going waveform with a latency of about 300 ms post stimuli. It is often elicited with an oddball paradigm, given that the single stimulus is presented in a random series where one of them occurs infrequently (Polich & Kok, 1995). P300 is recorded at the midline (Fz, Cz, Pz) and normally increases in magnitude from frontal to parietal electrodes (Polich & Kok, 1995). The neural generators of P300 are not clearly defined, although important progress has been made. It has been suggested that the P300 component is generated at the temporal-parietal junction (Polich, 2007).

P300 is considered to reflect an information processing cascade when attention and memory mechanisms are activated (Polich, 2007). In this regard, the amplitude of P300 is sensitive to the amount of attentional resource allocation, and its latency represents the speed with which attention resources are assigned (Polich, 2007). Although the P300 component frequently is viewed in the cognitive context, substantial research suggests that P300 represents higher-order phases of processing of emotional stimuli (Luo et al., 2010). Specifically, P300 amplitude reflects further evaluation of information related to the affective valence of a face. The emotional processing shown in this component is sensitive to attentional resource availability (Luo et al., 2010).

1.5.3 LPP component

ERP assessment of the temporal evolution of emotional processing begins, as mentioned previously, with early perceptual processing, and it continues in later stages involving elaborate processing and sustained attention. The LPP component has been widely used to assess the late stages of emotional processing because LPP reflects sustained and motivated attention and an

elaborated and controlled processing of the stimuli (Schupp et al., 2006). The LPP is a slow positive potential that typically occurs around 400-600 ms post-stimulus and reaches its maximum in centro-parietal regions (Schupp et al., 2006). Furthermore, LPP has also been utilized as a neural index of emotional reactivity and regulation (Proudfit et al., 2014).

It has been reported that emotional images elicit enhanced LPP. These results were found using emotional adjectives (Bartussek et al., 1996), faces (Schindler & Bublatzky, 2020; Van Strien et al., 2010), or pictures from the International Affective Picture System (IAPS; Schindler & Bublatzky, 2020). Interesting evidence of coordination has been found between LPP amplitude, the autonomic system, and subjective affective experience (Bradley, 2009). In this vein, enhanced LPP amplitude to pleasant and unpleasant images was related to self-reported arousal assessments and skin conductance response (Cuthbert et al., 2000). This evidence supports the concept of LPP as an indicator of sustained allocation of attention to the emotional stimulus and bottom-up processing (Hajcak & Foti, 2020; Olofsson et al., 2008).

It is known that emotional content conveys information about potential threats and opportunities that are important for survival. From a biological perspective, increases in LPP amplitude would reflect the relevance of the emotional stimulus for survival. Emotional content captures attention and facilitates approach or avoidance action tendencies (Hajcak & Foti, 2020). Bradley (2009) argued that LPP is a neural marker that indicates that cortico-limbic appetitive and defensive systems that mediate the sensory and motor have been activated. In this regard, specifically, the amplitude of the LPP would be an indicator of the importance of the stimulus. Thus, higher amplitude reflects further evaluation of information related to the affective valence of a face.

From a cognitive perspective, LPP amplitude would indicate the representation of stimuli in working memory (Schupp et al., 2006), improved recognition memory performance (Olofsson et al., 2008), and a gateway to conscious recognition (Luck et al., 2000).

1.6 RESTING STATE EEG

In contrast to ERPs, the recording of the resting state EEG rhythms does not require stimulation, and it is not influenced by fatigue, meta-learning, or the anxiety usually associated with task performance (Babiloni et al., 2016). Resting state electroencephalographic rhythms are often recorded from the person's scalp during short (i.e., minutes) eyes open (EO) and eyes closed (EC) conditions. In these conditions, individuals are instructed to maintain quiet wakefulness and vigilance (Babiloni et al., 2020a). This research is mainly focused on abnormalities in the frequency and topographical features of EEG rhythms that reveal neural dysfunctions in quiet wakefulness. Vigilance dysregulations may affect cognitive functions such as attention (i.e., focused, sustained, selective, or reflexive), episodic memory (i.e., encoding and retrieval of autobiographical events), and EF (i.e., working memory and inhibitory control; Babiloni et al., 2020a).

The common measures used to describe oscillatory signals are spectral power of frequency bands, EEG reactivity, and APF (Alexander et al., 2006; Lejko et al., 2020; Ruiz-Gómez et al., 2018), which experience gradual changes during normal and pathological aging (Alexander et al., 2006; Scally et al., 2018; Vysata et al., 2012). Spectral power of frequency bands and EEG reactivity in different frequency bands are involved in various cognitive processes (Başar et al., 2001; Engel & Fries, 2010). Spectral power is proportional to the rate of energy change at a specific frequency or frequency band, and it is involved in various cognitive processes such as attention, alertness, memory (encoding and retrieval), and

associative learning (Ward, 2003). Frequency bands range from slow, delta (0.5-4 Hz), and theta (4-8 Hz), to fast, alpha (8-12 Hz), beta (13-30 Hz), and gamma (>30 Hz). The activity in each of these bands has been associated with changes during healthy aging (Vysata et al., 2012) and dementia (Babiloni et al., 2020b; Lejko et al., 2020).

Research on resting EEG in older people reveals decreases in delta and theta bands (Babiloni et al., 2006) and reduced alpha power (Rossini et al., 2007), whereas activity in the beta band seems more controversial due to inconsistent findings (Barry & De Blasio, 2017; Wang et al., 2016). Specifically, patients with MCI and AD present an increment in delta or theta and a decrement in the alpha and beta bands (Babiloni et al., 2012; Hatz et al., 2013; Michels et al., 2017; Wan et al., 2018) compared to healthy older. Likewise, previous EEG investigations on SMCs have reported similar decreases in the theta band (Alexander et al., 2006; Babiloni et al., 2010), but contradictory findings in the alpha and beta bands (Alexander et al., 2006; Babiloni et al., 2010).

EEG reactivity or alpha blocking has been suggested as a neurophysiological marker of cognitive health, and it will be defined as the power difference in a frequency band between two different conditions: EO and EC (Klimesch, 1999). In the following, EEG reactivity is understood as the logarithm of the power in each band during the EO condition minus the logarithm of the power in the EC condition (Alexander et al., 2006). Generally, findings for EEG reactivity are being limited to the alpha band and has been suggested as a potential marker of activity of cholinergic system (Schumacher et al., 2020). In this regard, alpha reactivity was found to be decreased in people with MCI (Fröhlich et al., 2021) and AD (Chae et al., 2020) compared with healthy people.

Another promising variable that could help to improve the understanding of SMCs is an alpha band variant, known as APF, which was defined as the frequency showing its power

peak within the extended alpha range (8-12 Hz). It has been shown that APF shows remarkably high heritability and so is probably under strong genetic control (Klimesch, 1999). Given the high stability of interindividual differences, APF may be a valuable marker for monitoring deviations from normal central nervous system functioning, such as disease progression, by following within-person changes over time (Grandy et al., 2013b). Some studies showed robust evidence of EEG alpha band changes in their peak frequency and/or amplitude in physiological aging and AD progression (Garcés et al., 2013; Ruiz-Gómez et al., 2018). More specifically, a slowing of alpha in MCI has been found and established that age, sex, and hippocampal volume affect maximal amplitude and peak frequency of the alpha band (Garcés et al., 2013). In this line, a previous study observed that MCI patients exhibited a significantly lower APF compared to controls, and significantly higher APF compared to AD (Fernández et al., 2006).

As can be seen, resting-state EEG measurements are quite promising because they are non-invasive, reproducible (without learning effects) up to severe dementia, cost-effective, and based on recording techniques that are widely available worldwide. However, no comprehensive review of this field is available to date. To fill this gap, a review on EEG measures for instrumental assessment, status monitoring, and progression of SMCs is being prepared.

CHAPTER 2.
OBJECTIVES AND HYPOTHESES

Based on the inconsistent results and the questions in the literature presented in the introduction chapter, the current thesis will address the general and specific objectives and hypotheses presented below:

General objective 1. Examine whether facial emotion processing is different in young people with and without SMCs who were exposed to positive, negative, and neutral faces, by recording the ERPs activity and behavioral data.

Specific objective 1.1: Investigate differences in behavioral data (i.e., reaction time [RT] and accuracy) in young people with and without SMCs.

Specific objective 1.2: Study differences in latencies and amplitudes of N170 and LPP components in young people with and without SMCs.

Specific objective 1.3: Explore the possible sex-related differences in the processing of facial emotion between young people with and without SMCs.

Because the processing of facial emotions has not been addressed in young people with SMCs, we base our hypotheses on a hypothetical model about the cognitive functions involved in the processing of emotional faces (Luo et al., 2010). This model proposes that the processing of the emotional expression of the faces can be modulated by attentional resources. Thus, when attentional resources are abundant, higher amplitudes and shorter latencies are observed. Given that previous research has found attention difficulties in young people with SMCs (Ruiz-Sánchez de León et al., 2010), we expected longer latencies and smaller amplitudes in both the N170 and LPP components in participants with SMCs, compared to those without SMCs. We also hypothesized faster recognition times, better accuracy, shorter latencies, and greater N170 and LPP amplitude in women than in men, as has been reported in previous studies (Choi et al., 2015; Hampson et al., 2006; Sun et al., 2017).

Data and results obtained responding to these research objectives are presented in Chapter 3.

General objective 2. Investigate whether there are differences in the neuronal correlates and behavioral measures of facial emotion processing and its relationship with EF in older people with SMCs.

Specific objective 2.1: Study differences in behavioral measures (i.e., RT, and accuracy) in older people with and without SMCs.

Specific objective 2.2: Analyze differences in latencies and amplitudes of N170, P300, and LPP components in older people with and without SMCs.

Specific objective 2.3: Explore the possible associations between N170, P300, and LPP amplitudes and EF performance, assessed with various neuropsychological tests, in older people with and without SMCs.

Specific objective 2.4: Investigate the possible sex-related differences in the processing of facial emotion between older people with and without SMCs.

Based on previous studies carried out in MCI, we hypothesized that older people with SMCs would show a slower RT and worse accuracy compared to the control group (Sarabia-Cobo et al., 2015; Schefter et al., 2012). Additionally, we also anticipated differences in ERPs. Specifically, we expected longer latencies and smaller amplitudes in N170, P300, and LPP in SMCs participants compared to controls (Asaumi et al., 2014; Schefter et al., 2013; Yang et al., 2015). Because the association between EF and ERPs has not been previously studied in older people with SMCs, we did not have a hypothesis for this association. Finally, given that psychological (Montagne et al., 2005) and physiological (Choi et al., 2015; Li et al., 2008) studies have shown sex differences in facial emotion processing, we explored possible sex-related differences in the SMCs and control groups.

These objectives will be addressed in Chapter 4 of this thesis.

General objective 3. Investigate whether resting-state EEG rhythms and EEG reactivity, usually altered in MCI and AD, are also affected in older and young people with SMCs in comparison with control people.

Specific objective 3.1: Determine the EEG spectral power of frequency bands in older and young people with and without SMCs.

Specific objective 3.2: Analyze EEG reactivity to EO in older and young people with and without SMCs.

Specific objective 3.3: Explore whether there is a correlation between the region and specific spectral and EEG reactivity and neuropsychological measures.

We formulated several working hypotheses based on previous studies on MCI and AD patients. We proposed that the cortical EEG rhythms, usually altered in MCI and AD (i.e., decrease in fast waves and increase in slow waves), would also be affected in SMCs when compared to control people, as possible early markers 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., 2011; Fröhlich et al., 2021). Finally, we hypothesized that an alteration in resting-state EEG would be correlated with worse cognitive function (Babiloni et al., 2012; Gaubert et al., 2019).

Chapter 5 aims to respond to these specific research objectives.

General objective 4. Investigate the alpha peak parameters, such as APF and amplitude, in SMCs and control people. Furthermore, we explored whether these parameters not only differ between SMCs and controls, but also between young and older people, as well as by sex.

Specific objective 4.1: Examine the APF and alpha amplitude in SMCs and control people.

Specific objective 4.2: Investigate the possible differences between young and older people, as well as sex-related differences in the APF and alpha amplitude.

Specific objective 4.3: Explore whether there is relationship between CR and APF and alpha amplitude in the context of SMCs in each age group (older and young).

Based on previous literature in MCI and AD, we hypothesized that older people with SMCs would also show lower APF and reduced amplitude compared to their matched controls (et al., 2013; Ruiz-Gómez et al., 2018). Furthermore, in the context of age-related physiological differences, alpha peak parameters might be slowed down, as reported in a previous study (Scally et al., 2018). Because sex-related differences in people with SMCs have not yet been determined, we did not have specific hypotheses about this. Finally, although the study of the relationship between CR and APF and amplitude has not been carried out to date, we examined this correlation because CR has shown protective effects against cognitive impairment (Lojo-Seoane et al., 2018).

We aimed to respond to these research objectives in Chapter 6.

CHAPTER 3.
FACIAL EMOTION PROCESSING IN YOUNG PEOPLE WITH SUBJECTIVE MEMORY COMPLAINTS

The main results of this chapter have been published in: Perez, V., Garrido-Chaves, R., Perez-Alarcón, M., Paiva, T. O., Pulopulos, M. M., Hidalgo, V., & Salvador, A. (2021). An ERP study on facial emotion processing in young people with subjective memory complaints. *Scientific Reports*, 11(1), 1-9. https://doi.org/10.1038/s41598-021-90861-9

3.1 INTRODUCTION

SMCs have been defined as subjective awareness of memory loss in the absence of any organic or identifiable condition in neuropsychological examinations (Schmand et al., 1996). A previous review pointed out that the prevalence of SMCs among older people ranges from 25 to 50%, depending on the assessment method and the population´s characteristics (Iliffe & Pealing, 2010). In Spain, the prevalence of SMCs was 32.4 % in a study conducted with older people in Madrid (Montejo et al., 2011), which is similar to the prevalence observed in a large community-based study in Australia (Mewton et al., 2014). However, although memory complaints are frequently reported by older people, the available evidence indicates that SMCs are also reported by young adults (Ginó et al., 2010; Lozoya-Delgado et al., 2012). A study carried out in the UK reported that the prevalence of SMCs increased with age, and 5.5% to 6.3% of people between 16-24 years old reported SMCs (Begum et al., 2013). As in older people, research in young people has shown that SMCs are not associated with objective memory performance (Molina-Rodríguez et al., 2016; Stocker et al., 2017). However, SMCs have been related to attention and executive difficulties (Ruiz-Sanchez de Leon et al., 2010), perceived stress (Molina-Rodríguez et al., 2016, 2018) and anxiety symptoms (Derouesné et al., 1999; Montenegro et al., 2013; Pellicer-Porcar et al., 2014) in young adults, and to depression in a mixed-age sample (Mendes et al., 2008). In this regard, it is important to investigate the mechanisms that may contribute to an increased perception of stress and even the development of stress-related disorders, such as anxiety and depression, in young adults with SMCs.

Facial emotion processing is a complex process that involves many cerebral structures, including the amygdala and occipitotemporal cortex and, particularly, the orbitofrontal cortex (Eimer & Holmes, 2007). The latter region is known to play an important role in attention to emotional stimuli (Sander et al., 2005). Taking into account that correct facial emotion

processing is necessary for successful human interactions (McCade et al., 2011), its impairment could at least partly contribute to the development of stress-related disorders reported in people with SMCs (Metternich et al., 2009; Yoon et al., 2016; Zhao et al., 2015). In addition, facial emotion processing is an important source of knowledge about the emotions of others and social information (for a review see: (Hinojosa et al., 2015) that is commonly affected in older people with SMCs (Lazarou et al., 2018; Pietschnig et al., 2015). The ability to efficiently recognize emotional facial expressions correlates with problem-solving capacity and facilitates social interactions and adequate adaptation to a new environment (Poncet et al., 2019; Soto et al., 2018). Moreover, some studies have shown that, in disorders related to cognitive impairment, deficits in the facial emotion processing ability influence social behavior (e.g., the ability to perceive and recognize the affective state of others; Elferink et al., 2015; Spoletini et al., 2008). Along these lines, previous studies have shown a relationship between attentional bias toward negative stimuli and anxiety (Pan et al., 2019; Yoon et al., 2016), long-term stress (Zhang et al., 2016), and depression (Zhao et al., 2015) in young people. Therefore, investigating deficits in facial emotion processing in young people with SMCs may be interesting because it would help to understand the development of stress-related disorders and provide potential evidence of difficulties in attending to emotional stimuli in this population.

Facial emotion processing can be analyzed by ERPs (Hinojosa et al., 2015), which are considered reliable biomarkers of cognitive operations (Lazarou et al., 2018) that allow the assessment of neural reactivity to affective events with a high temporal resolution (Olofsson et al., 2008). Electrophysiological data reveal that ERPs are sensitive to the emotional content of facial expressions in early stages of emotional processing (Hinojosa et al., 2015). More specifically, the main components related to faces and facial emotion processing are the N170 (Hinojosa et al., 2015) and the LPP (Zhao et al., 2015). The N170 component is an early negative component that is detected at 120-200 ms and peaks at approximately 170 ms post-

stimulus, which has been proposed as a correlate of the interpretation of a visual stimulus such as a face, although it can be induced by other objects consciously interpreted as face-like (e.g., pareidolia; Bentin et al., 1996; Rossion, 2014). Located primarily in the occipitotemporal brain region, the N170 usually shows a greater response over the right hemisphere than over the left hemisphere (Sato et al., 2017), and it can be modulated by emotion processing (Blau et al., 2007). Importantly, Lazarou et al. (2018), in their study on negative faces (anger and fear), demonstrated that older people with SMCs show larger N170 amplitudes to negative faces than healthy controls. The LPP component is a slow positive potential that occurs at approximately 400-600 ms post stimulus onset, with a maximum peak at the midline central and parietal electrodes, and it shows higher amplitudes for emotional images than for neutral images (Schupp et al., 2000; Van Strien et al., 2010), which represents sustained attention (Yoon et al., 2016). This component reflects brain electrical activity during both automatic and controlled attentional processing for emotional information, and it indicates more elaborate emotion-related processing, such as high-level recognition processing (Moran et al., 2013; Sun et al., 2017). To the best of our knowledge, no previous studies have investigated the LPP component on a facial emotion processing task in people with SMCs.

With all this in mind, the present study aimed to investigate whether facial emotion processing is different in young people with and without SMCs who were exposed to positive, negative, and neutral faces. To do so, we employed the two main components of processing usually studied in this context, and we also included behavioral data (RT, and accuracy). Given that higher amplitudes and shorter latencies are observed when attentional resources are abundant, and that processing in the N170 and LPP is sensitive to attentional resources (Luo et al., 2010), we expected longer latencies and smaller amplitudes in both the N170 and LPP components in participants with SMCs, compared to those without SMCs. Finally, sex-related differences in facial emotion processing have been found, with faster recognition times, better

accuracy, shorter latencies, and greater N170 and LPP amplitude in women than in men (Choi et al., 2015; Hampson et al., 2006; T. Sun et al., 2017). Therefore, we included both women and men in order to explore possible sex-related differences in young people with and without SMCs.

3.2 MATERIAL AND METHODS

3.2.1 Participants

Eighty healthy young students participated in the study (41 men, 39 women; mean age = 22.1 years; Table 3.1). Participants were recruited at the University of Valencia campus (Spain). Undergraduates who met the criteria were contacted by telephone and asked to attend a session that took place in the Laboratory of Social Cognitive Neuroscience.

The exclusion criteria were: history of alcohol or drug abuse; smoking more than 10 cigarettes a day; having had surgery under general anesthesia in the past year; presence of severe vision or hearing problems or an illness that involves an alteration of the nervous system; and a neurological or psychiatric disorder. In addition, participants were excluded if they took drugs that might affect cognitive or emotional function, psychotropic substances, beta-blockers, or benzodiazepines, or if they had experienced a stressful event in the past six months. All the participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971).

Participants were distributed into two groups: SMCs (N=41; 20 men and 21 women) and no SMCs (noSMCs) (N= 39; 21 men and 18 women), according to the scores obtained on the Spanish adaptation (Lozoya-Delgado et al., 2012) of the modified version of (MFE-30) questionnaire (Sunderland et al., 1984). This questionnaire consists of 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). We employed these scores to distribute participants into two groups according to the scores obtained on this questionnaire. The participants who scored equal to or below 21 were included in the noSMC group, whereas the participants who scored above 21 were included in the SMCs group (descriptive data for each condition and sex group are summarized in Table 3.1).

The study was carried out according to the Declaration of Helsinki, and the Ethics Committee of the University of Valencia approved the protocol. All the participants received verbal and written information about the study and signed an informed consent.

Table 3.1. Demographic data (mean and SD) for each group and sex.

	SMCs	noSMCs	Men	Women
Age (years)	21.17 (3.27)	23.22 (4.0)	22.87 (3.89)	21.46 (3.53)
BMI (Kg/m^2)	21.93 (3.26)	23.16 (3.89)	23.10 (3.96)	21.96 (3.17)
SES	5.7 (1.22)	6.0 (1.14)	6.0 (1.20)	5.71 (1.16)

Notes: BMI = Body Mass Index; SES =Socioeconomic Status; SMCs = Subjective Memory Complaints.

3.2.2 Procedure

Participants arrived at the laboratory, and the experimenter verified that they had followed the instructions given before the experiment: sleep as long as usual, refrain from heavy physical activity the day before the session, and not consume alcohol or any stimulants since the night before the session.

The experimental session took 2 h and was carried out in the morning (between 10 and 14:00 h) or in the afternoon (between 15:00 and 19:00 h). Half of the participants attended the morning shift, and the other half attended the afternoon shift. There were no differences in the number of participants in each group in each shift ($\chi^2 = 2.8,\ p = 0.423$).

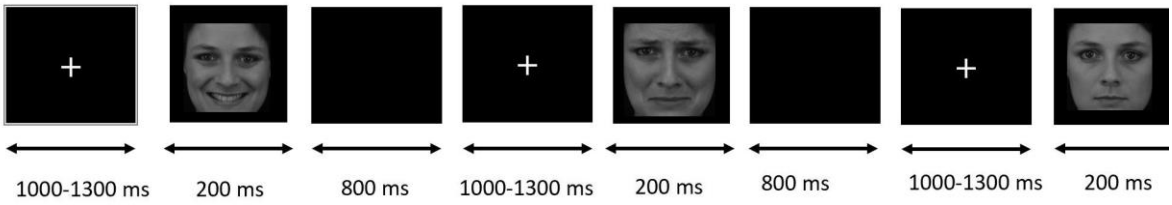
The session started with a period of habituation to the laboratory lasting 15 min. Then, the participants were prepared for the EEG register (10 min) and performed two blocks of resting EEG collection (i.e. closed eyes and opened eyes) for three minutes each block. Next, the face stimulus task was presented, which lasted 12 min. After the task, weight and height were measured, and then the participants had 40 min to answer the MFE-30 and a General Questionnaire where demographic data were collected. As part of a larger research project not related to the research question of the current study, the participants completed other cognitive tasks and questionnaires (data not included here).

3.2.3 Face Stimulus task

Images of human facial expressions with positive, negative, and neutral valences were used as stimuli. Each valence contained 68 images. All the images were adapted from a standard set of pictures to generate emotional stimuli (Lundqvist et al., 1998). Images of men and women and the valences of the images were presented randomly to the participants and in equal proportion. All the images were presented in grayscale on a black background and displayed in the center of a 24-inch screen.

The stimuli were presented in the following sequence: (1) a fixation mark (+) appeared for 1000 to 1300 ms; (2) the face was presented for 200 ms; and (3) a blank screen was displayed for 800 ms (Figure 3.1). The images were presented using the E-prime program (v2.0). Participants were instructed to press the 1 key if the facial expression was positive, 2 if it was negative, and 3 if it was neutral. The participants were seated 70 cm from the screen in a dimly lit and sound attenuated room. The task started with practice trials containing 12 images. Each participant received feedback after each of these 12 trials, indicating whether he/she had done it correctly or incorrectly.

Figure 3.1. Timeline of events during the session



Copyright: https://kdef.se/home/using%20and%20publishing%20kdef%20and%20akdef.html

Note: ms = milliseconds. The images are an example of faces of each emotion extracted from the Karolinska Emotional Directed Faces database. Image ID: AF01DIS, AF01ANS, AF01NES.

3.2.4 ERP recording and data analyses

The EEG data were collected using an elastic cap from a 29-channel system, according to the international 10–20 system (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, M1, T3, C3, Cz, T4, C4, M2, T5, P3, Pz, P4, T6, O1, OZ and O2), using a Brain Vision Amplifier System (Brains product, Germany). The electrode AFz was used as the system ground, and electrodes were referenced to Fcz. Both vertical and horizontal electro-oculograms were captured by additional electrodes (VEOG-, VEOG+, HEOG-, HEOG+) placed around the eyes. The electrode-to-skin impedances were lowered using electrolyte gel (SUPER-VISC High Viscosity Electrolyte-Gel, EasyCap, GmbH), and they were kept below 5 kΩ before starting the recording. The BrainVision Analyzer (BrainProducts, Germany) was used to analyze the EEG data. Data were re-referenced to a common average signal of 23 electrodes (Joyce & Rossion, 2005). The EEG and EOG were amplified and then passed through (0.1Hz - 30 Hz) band-pass filtering using an IIR filter (24 db/octave roll-off). One-second epochs were extracted in a range from -200 to 800 ms. Epochs were then corrected to the mean voltage of the baseline −200. Trials with EOG artifacts, including blinking, eye movement, and skin potentials, were corrected offline with the algorithm from Gratton and Coles (Gratton et al., 1983), and trials with wrong answers were removed from averaging. Based on the overall mean chart, the early ERPs component

(i.e. N170) generated by the stimuli showed clear peaks. A time window of 130-200 ms was used to measure the ERPs peak and peak latency in data collected at electrode sites T6 (right temporal lobe) and T5 (left temporal lobe) for N170. The LPP component was calculated at the Pz electrode, with a mean value of the amplitude within a 400–700ms time-window.

3.2.5 Statistical Analyses

For behavioral performance, RT and accuracy were analyzed using ANOVAs for mixed-designs, with Emotional Valence (positive, negative, and neutral) as a within-subject factor and Sex (men and women) and Group (SMCs and noSMCs) as between-subject factors.

To study the amplitudes and latencies of the N170 and LPP components, we carried out ANOVAs for mixed-designs, with Emotional Valence (positive, negative, neutral) as a within-subject factor and Sex and Group as between-subject factors. In the analyses with N170, Hemisphere (Right and Left) was also included as a within-subject factor.

In cases of violation of sphericity, Greenhouse-Geisser correction was applied. Post-hoc planned comparisons were performed using Bonferroni adjustments for the p values. The level of significance was taken as $p = 0.05$. There were no outliers (± 3SD) in this study. We used SPSS 24.0 to perform the statistical analysis.

3.3 RESULTS

3.3.1 Behavioral performance

Table 3.2 shows RT and accuracy. For RT, a significant effect of Emotional Valence, F (1.963, 149.189) =204.095, $p = 0.001$, $\eta p^2 = 0.729$, was found. RT were shorter for positive faces than for negative and neutral faces (both $p < 0.001$), and shorter for negative faces than for neutral ($p = 0.005$) faces. Neither the Sex ($p = 0.627$) and Group ($p = 0.349$) factors nor their interactions were significant (all $p > 0.994$).

For accuracy, a significant effect of Emotional Valence, F (1.973, 149.964) = 51.899, $p < 0.001$, $\eta p^2 = 0.406$, was found. Thus, accuracy was higher for positive faces than for negative and neutral faces (both $p < 0.001$), and it was higher for neutral faces than for negative faces ($p = 0.003$). Neither the main effects of Sex ($p = 0.190$) and Group ($p = 0.089$) nor the rest of the interactions reached statistical significance (*ps* > 0.542).

Table 3.2. Means and standard deviations for the behavioral performance for each group and sex.

Reaction time (ms)	SMCs	noSMCs	Men	Women
Positive	684.7 (75.8)	664.8 (86.8)	669.6 (79.3)	680.7 (84.4)
Negative	807.6 (85.2)	789.8 (107.4)	798.3 (88.0)	799.6 (102.7)
Neutral	833.6 (99.3)	813.8 (116.7)	814.6 (107.2)	833.7 (109.2)
Response accuracy (%)				
Positive	94.6 (2.9)	95.8 (2.0)	94. 9 (2.9)	95.6 (2.1)
Negative	77.5 (11.5)	79.7 (5.9)	79.5 (6.4)	77.6 (11.5)
Neutral	80.5 (14.0)	87.8 (6.4)	87.6 (5.7)	80.3 (14.6)

Notes: ms = milliseconds; SMCs = Subjective Memory Complaints.

3.3.2 ERP data analysis

3.3.2.1 N170 component

For N170 latencies, the analyses revealed that the Emotional Valence, F (1.955, 136.858) = 1.553 $p = 0.216$, $\eta p2 = 0.216$, Hemisphere, F (1,70) = 0.615 $p = 0.436$, $\eta p2 = 0.009$, Sex, F (1, 70) = 0.353 $p = 0.554$, $\eta p2 = 0.005$, and Group, F (1, 70) = 1.338 $p = 0.251$, $\eta p^2 = 0.019$, factors were not significant. The Emotional Valence x Group interaction, F (1.955, 136.858) = 3.256 $p = 0.043$, $\eta p^2 = 0.044$, was statistically significant; however, post hoc comparisons did not show significant differences (all *ps* > 0.926) (Fig. 3.2.a). The Emotional Valence x Hemisphere x Group x Sex interaction was also significant, F (1.878, 131.4556) = 3.226 $p = 0.046$, $\eta p^2 = 0.044$. Post hoc analyses revealed that women SMCs showed longer latencies in the right hemisphere for neutral faces than women noSMCs ($p = 0.005$). None of

the other post hoc analyses revealed significant effects (all *ps* > 0.082). The other interactions were not significant (*ps* > 0.764).

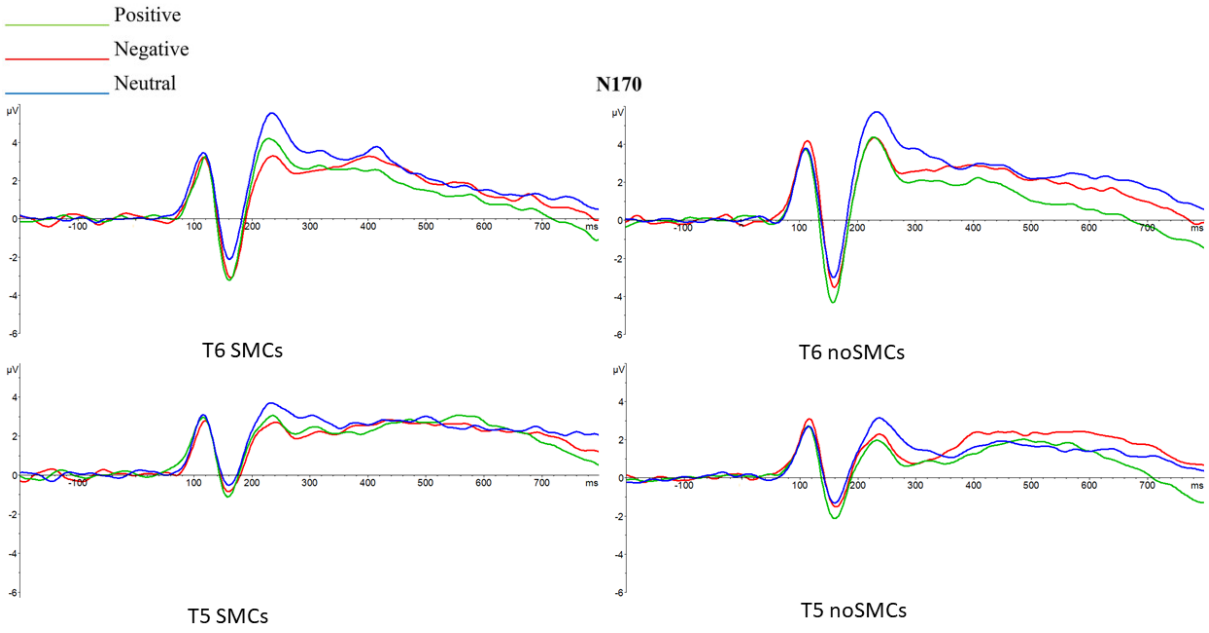
For N170 amplitudes, the effect of Emotional Valence was significant, F (2, 140) = 21.274 $p = 0.001$, $\eta p^2=0.233$, with higher amplitudes for positive faces than for negative *(p* = 0.049) and neutral ($p = 0.001$) faces, and higher amplitudes for negative faces than for neutral ($p = 0.001$) faces. The Group factor was also significant, F (1, 70) = 4.563 $p = 0.036$, $\eta p^2=0.061$, indicating that SMCs participants showed less amplitude than noSMCs. In addition, a significant effect of the Emotional Valence x Group interaction, F (2, 140) = 5.331 $p = 0.006$, $\eta p^2=0.071$, was found. Post hoc comparisons revealed that the SMCs participants showed lower amplitudes than noSMCs for positive ($p = 0.007$) and neutral ($p = 0.050$) faces, but not for negative faces ($p = 0.148$) (Fig. 3.2.a).

We also found a significant effect of the Hemisphere, F (1, 70) = 17.550 $p < 0.001$, $\eta p^2=0.200$, and Sex, F (1, 70) = 4.200 $p = 0.044$, $\eta p^2=0.057$, factors (Fig. 3.2.b). Thus, we observed higher amplitude in the right hemisphere than in the left hemisphere, and men showed less amplitude than women. Other interactions were not statistically significant (*ps* > 0.711).

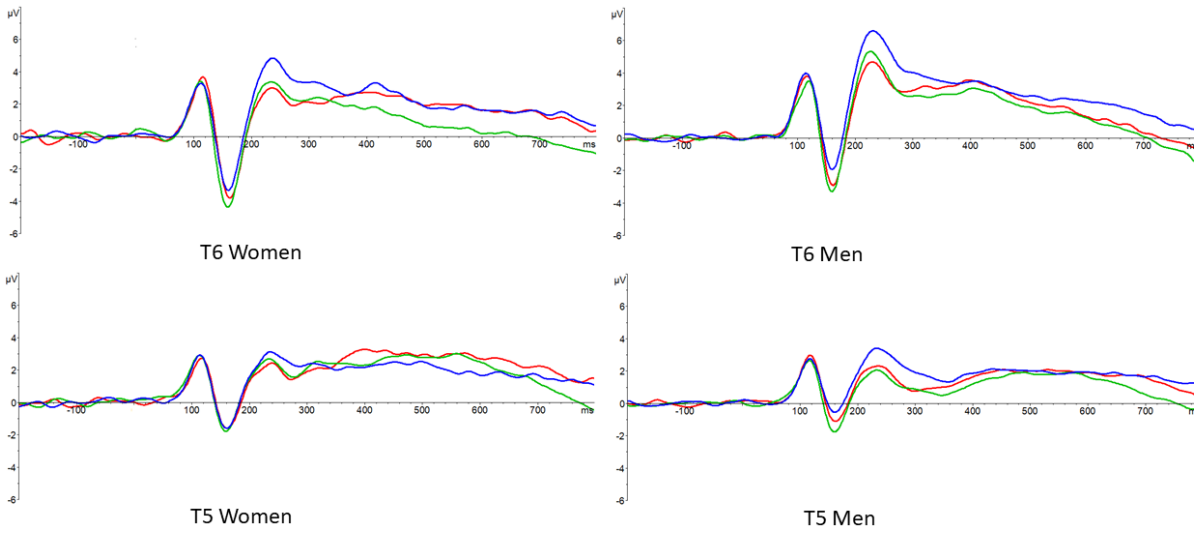
Figure 3.2. Latencies and amplitudes of N170 and LPP induced by groups and sex.

(**a**) Grand average N170 for positive (green), negative (red), and neutral (blue) faces recorded in the right and left hemisphere in young people with and without subjective memory complaints. (**b**) Grand average N170 for positive, negative, and neutral faces recorded in the right and left hemisphere in young women and men.

a)



b)



3.3.2.2 LPP component

For LPP latencies, results showed a significant effect of Emotional Valence, F (2, 136) = 9.475 $p < 0.001$, ηp^2=0.122. LPP latency was shorter for positive faces compared to neutral ($p = 0.001$) faces, and shorter for negative faces compared to neutral ($p = 0.034$) faces. Other effects or interactions were not significant ($ps > 0.614$).

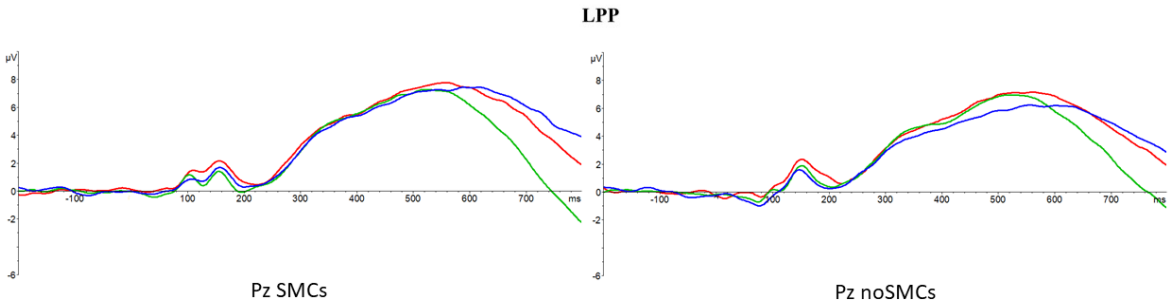
For LPP amplitudes, the Emotional Valence was significant, F (1.912, 131.924) = 5.431 $p = 0.006$, ηp^2=0.073. Post hoc comparison revealed that amplitudes were significantly higher for negative faces than for positive ($p = 0.003$) faces, but no other significant differences were found (all $p > 0.232$) (Fig. 3.2.c).

In addition, the Sex factor was significant, F (1, 69) = 5.261 $p = 0.025$, ηp^2=0.071, with men showing smaller LPP amplitudes than women. Other effects and interactions were not significant ($ps > 0.827$) (Fig. 3.2.d).

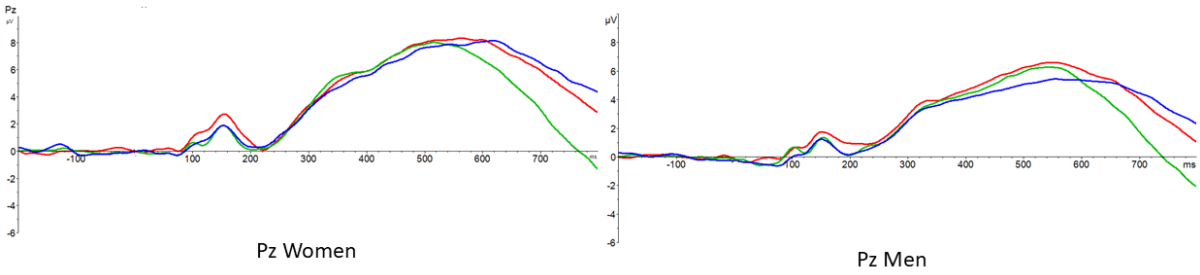
Figure 3.2. Latencies and amplitudes of N170 and LPP induced by groups and sex

(c) Grand average LPP for positive, negative, and neutral faces in young people with and without subjective memory complaints. **(d)** Grand average LPP for positive, negative, and neutral faces recorded in young women and men.

c)



d)



3.4 DISCUSSION

The aim of the present study was to investigate whether facial emotion processing (i.e. positive, negative, and neutral faces) is different in young women and men with SMCs compared to other groups without SMCs. At the behavioral level, only positive valences showed clearly significant effects on both RT and accuracy, with no significant differences due to SMCs or sex. Regarding ERPs, we found that participants with SMCs showed lower amplitudes than noSMC participants in the N170 component, specifically for positive and neutral faces. In addition, women with SMCs showed longer latencies in N170 for neutral faces compared to women noSMCs. For the LPP component, no differences depending on SMCs were found for latency and amplitude. Notably, the participants showed higher amplitudes for negative faces. Finally, we observed that women showed higher amplitudes than men for both the N170 and LPP components, although no differences in latencies were found.

Regarding behavioral data, neither RT nor accuracy was significantly different between the SMCs and noSMCs groups, indicating similar performance for both groups. This lack of differences between groups in the behavioral data is consistent with a previous study carried out in controls and older people with SMCs (Pietschnig et al., 2015). Regardless of the group and sex, participants showed less latency and more accuracy for positive expressions, and they were slower for neutral faces and less accurate for negative faces. Complementary to this, Calvo and Lundqvist (2008) demonstrated that positive expressions have a salient and unique

facial feature, the smile, which allows quick and accurate identification. By contrast, negative or neutral expressions contain more overlapping features, which would generate confusion, making the decision process slower (Calvo & Lundqvist, 2008).

Although there is debate about the meaning of the N170 component, it may be considered a neural indicator of facial structure encoding (Bentin et al., 1996; Sagiv & Bentin, 2001), where the structural representation of the face is associated with the necessary semantic information to form an internal representation of a human face (Sagiv & Bentin, 2001), combining both bottom-up and top-down processes. In addition to structure encoding, the N170 is also involved in facial emotion processing, especially for the early processing of the emotional valence (Qiu et al., 2017). In this vein, the smaller amplitude elicited in N170 by the SMCs group compared to the noSMCs group might reflect emotional processing difficulties in this stage of processing in this population. Moreover, on closer examination, the N170 amplitude was lower for positive and neutral faces in SMCs than in noSMCs, whereas negative faces elicited similar amplitudes in both groups. From a biological point of view, a possible interpretation of this pattern of processing of negative faces could have an adaptive function, given that negative face recognition is more relevant because these expressions are signs of potential harm (Calvo & Beltrán, 2013). To the best of our knowledge, no previous studies have investigated the N170 component with positive, negative, and neutral faces together in relation to SMCs. One study carried out in older people with a diagnosis of SMCs, Alzheimer disease, mild cognitive impairment, and healthy older participants only focused on negative stimuli to capture any cognitive changes (Lazarou et al., 2018). These authors found larger N170 amplitudes in response to faces showing fear in SMCs than in healthy participants, suggesting that an increase in N170 amplitudes reflects the difficulty in computing spatial relations among face features and understanding the different negative emotions of facial expressions. However, these results must be interpreted with caution because some studies

have indicated that low amplitudes (in regions involved in face processing, particularly in frontal and temporal areas) would be related to a decline in emotion processing (Ruffman et al., 2008). Furthermore, because this study only takes negative facial stimuli into consideration, its results may not be used for comparisons with positive or neutral stimuli. We also found that there is right hemisphere dominance for N170 amplitude in both groups. This result supports evidence showing that neurons in the right superior temporal gyrus respond to the processing of facial expressions of emotion (Bentin et al., 1996; see review: Adolphs, 2002).

Regarding the LPP, we found no differences between the SMCs and noSMC groups in latency or in amplitude. However, regardless of the group, participants presented shorter latencies for positive faces than for negative and neutral faces, whereas the amplitude was greater for negative faces than for positive and neutral faces. This result is consistent with our behavioral data showing slower and less accurate responses for negative faces. In agreement with this, prior research suggests that positive faces are more easily processed in this late stage (Calvo & Beltrán, 2013). In addition, more attentional resources and greater cortical activation are allocated to negative faces than to positive and neutral faces in this stage of processing (Luo et al., 2010). This probably occurs because negative faces have greater biological relevance, and so the attention is directed toward these significant stimuli. In the present study, young people with SMCs showed a deficit in attentional resources only for early processing of facial positive and neutral emotions (N170), whereas both groups processed negative stimuli similarly. These findings are consistent with the hypothesis that the processing of potentially threatening stimuli may occur without attentional involvement (Luo et al., 2010). Together, our results suggest that young people with SMCs would not present difficulties in late processing, which involves a greater evaluation of the information related to the affective valence of a face (Luo et al., 2010); that is, sustained attention would be preserved.

The relationship between SMCs and facial emotion processing is complex and poorly understood. Some studies indicate that impaired emotional face processing affects quality of life and interactions in everyday social life (Elferink et al., 2015; Poncet et al., 2019). Consequently, impaired facial emotion processing can have a negative impact on social behavioral competence (McCade et al., 2011), and it could play an important role in the development of stress-related psychopathology in young people with SMCs.

Finally, we found that men showed smaller amplitudes for both the N170 and LPP components than women. Several studies have investigated the relationship between sex and facial emotion processing, but the results are mixed. Some did not observe sex differences (Verhallen et al., 2017), other studies indicated that advantages women have over men are only for female faces and not for male faces (for a review see: Herlitz & Lovén, 2014), whereas others observed sex differences (Proverbio, 2017). Our finding could suggest that, in general, women show a more sensitive attentional processing of emotional faces than men. In addition, this processing begins in the first stage and is maintained in the late evaluative process. This result is in line with studies that have shown that women are more responsive to face stimuli than men, which could suggest greater empathy or greater attention to facial features and more interest in social information (Proverbio, 2017).

Despite the relevance and novelty of our results, some limitations should be considered. First, further studies may benefit from investigating the effect of the arousal of emotional expressions when exploring the LPP component because valence mainly modulates the early stage of emotional processing, whereas arousal mainly modulates the late stage (for review see: Olofsson et al., 2008). Second, we used static and grayscale facial pictures as stimuli, and they subtract important lively information that people use to recognize facial expressions in natural contexts. In contrast, colors and three-dimensional stimuli provide a more real effect than our stimuli (Gur et al., 2002). Finally, the power analysis in G*Power showed that the sample size

is large enough to observe small to medium effect sizes (f=145; power=0.8, alpha=0.05) for the main aim of the study, that is, the Emotional Valence x Group interaction. In fact, the results of this interaction indicated a medium to large effect size (ηp^2=0.071, f=0.276). However, given that it is not possible to calculate the sample size needed to detect a triple interaction (i.e., Emotional Valence x Sex x Group), we can assume that we only have enough statistical power to detect large effect sizes. Therefore, the results of the exploratory analyses investigating sex-related differences should be interpretated with caution. Finally, despite some strengths of this study, such as the thorough selection of the participants and the sample size, the number of statistical analyses carried out calls for caution in interpreting the results obtained and emphasizes the need to replicate them (Luck & Gaspelin, 2017).

In conclusion, our study showed subtle differences in N170 amplitudes for positive and neutral faces, which suggest that young adults with SMCs have difficulties in the early stage of emotional processing. Importantly, these difficulties were not observed in behavioral performance or in the late stages of emotional processing, which suggests that sustained attention to emotional faces is preserved in this age group. Further studies investigating the course of facial emotion processing would help us to understand some difficulties that characterize this population and that could be the cause of greater vulnerability to developing subjective deficits and other stress-related disorders.

CHAPTER 4.
FACIAL EMOTIONAL VALENCE PROCESSING IN OLDER PEOPLE WITH SUBJECTIVE MEMORY COMPLAINTS

The main results of this chapter have been published in: Perez, V., Garrido-Chaves, R., Zapater-Fajarí, M., Pulopulos, M. M., Barbosa, F., Hidalgo, V., & Salvador, A. (2021). Deficits in facial emotional valence processing in older people with subjective memory complaints: Behavioral and electrophysiological evidence. *Psychophysiology*, e13989. https://doi.org/10.1111/psyp.13989

4.1 INTRODUCTION

In recent years, SMCs have received attention because they are considered a prodromic phase of mild cognitive impairment MCI; (Jessen, 2010) or AD; (Rönnlund et al., 2015). SMCs occur in the absence of any organic or identifiable condition in a medical or neuropsychological examination (Schmand et al., 1996). SMCs are frequently reported by older people (Burmester et al., 2015), with some studies showing a higher prevalence in women (Genziani et al., 2012) and others showing more SMCs in men (Holmen et al., 2013). Likewise, the relationship between SMCs and objective neuropsychological performance varies. Whereas some studies have reported no differences in neuropsychological performance (Peter et al., 2014; Van Flier et al., 2004;), others have related SMCs to worse neuropsychological functioning (Benito-León et al., 2010; Cespón et al., 2018; Stenfors et al., 2013; Vaskivuo et al., 2018). These latter studies have found that older people with SMCs have deficits in cognitive processes related to EF, such as working memory and attentional shifting (Stenfors et al., 2013), inhibitory control (Cespón et al., 2018), and phonologic fluency (Benito-León et al., 2010). Importantly, EF seems to be relevant in facial emotion processing (Ibáñez et al., 2011; Mathersul et al., 2009; Pessoa, 2009).

Facial expressions report how people feel and their tendency toward action (Yang et al., 2015). In this regard, the capacity to extract emotional states from facial expressions is a key component of social functioning (Hinojosa et al., 2015). Consequently, deficits in facial emotion processing affect everyday life and may underlie impaired social skills (Elferink et al., 2015). Despite this, few studies have been carried out on this issue in people with SMCs (Lazarou et al., 2018; Pietschnig et al., 2015), although several studies have examined pathologies characterized by cognitive decline, such as MCI (for review, see: McCade et al.,

2011; Schefter et al., 2013; Spoletini et al., 2008; Varjassyová et al., 2013; Yang et al., 2015) and AD (for review, see: Elferink et al., 2015; Fide et al., 2019).

Facial emotion processing is a complex process that involves different cerebral structures, such as the frontal and temporal areas (Ruffman et al., 2008), inferior occipital temporal cortex, fusiform gyrus (Eimer & Holmes, 2007), amygdala, orbitofrontal cortex, basal ganglia, and right parietal cortices (Adolphs, 2002). Facial emotion processing can be analyzed by using ERPs. Due to their excellent temporal resolution, ERPs provide insight into different stages of emotional processing, including early perceptual processes as well as later processes (Schefter et al., 2013). Regarding early perceptual processing, the N170 is a negative ERP component that peaks at approximately 150-170 ms and reflects the conscious interpretation of a stimulus such as a face (Hinojosa et al., 2015; Rossion, 2014). This component is distributed in the occipitotemporal cortex, with neural generators in the fusiform gyrus (Hinojosa et al., 2015; Sadeh et al., 20), and it can be modulated by the emotional valence (Qiu et al., 2017). Processing of the emotional valence is also reflected in late components known as P300 (Luo et al., 2010) and LPP; (Moran et al., 2013). The activity of the P300 component reflects cognitive processes such as memory encoding and attention, and it is one of the most widely studied (for a review, see Pavarini et al., 2018). Specifically, the amplitude of P300 is sensitive to the amount of attentional resource allocation, and its latency represents the speed with which attention resources are allocated (Polich, 2007). Previous studies reported that P300 latency was longer in older people with SMCs who performed different tasks, such as the Go/No-Go task (Smart et al., 2014), Simon task (Cespón et al., 2018), and auditory oddball task (Gironell et al., 2005). With broader latency than P300, LPP is a slow positive potential that becomes most apparent around 400 to 600 ms after the stimulus at centro-parietal midline sites (Schupp et al., 2006). Furthermore, LPP reflects sustained and motivated attention and an elaborate and controlled processing of the stimulus (Schupp et al., 2006). Specifically, increases in LPP

amplitude would reflect the representation of stimuli in working memory (Schupp et al., 2006) and improved recognition memory performance (Olofsson et al., 2008). A prior study reported reduced LPP amplitude in older adults with memory impairments during word encoding and recognition (Kenney et al., 2019). However, to the best of our knowledge, no previous studies have investigated the P300 and LPP activity in facial emotion processing in older people with SMCs.

Given that deficits in facial emotion processing have been widely studied in MCI, and that SMCs are considered a risk factor in developing MCI, we wonder if these deficits also occur in SMCs. Taking this into account, our main aim was to determine whether there are differences in the neuronal correlates and behavioral measures of facial emotion processing between older people with and without SMCs (SMCs and control groups, respectively). Based on previous studies in MCI patients, we expected a slower RT and worse accuracy in the SMCs compared to the control group (Sarabia-Cobo et al., 2015; Schefter et al., 2013; Yang et al., 2015) on a facial emotion processing task. We also expected longer latencies and smaller amplitudes in N170, P300, and LPP in SMCs participants compared to controls (Asaumi et al., 2014; Schefter et al., 2013; Yang et al., 2015). In addition, considering that difficulties in the processing of facial emotions have been related to EF deficits (Pietschning et al., 2016; Teng et al., 2007), a second aim was to investigate the possible association between ERPs measures and EF performance, assessed with several neuropsychological tests, in older people with and without SMCs. Finally, given that many psychological (Montagne et al., 2005) and physiological (Choi et al., 2015; Li et al., 2008) studies have shown sex differences in facial emotion processing, we included an equal distribution of women and men to explore possible sex-related differences in the SMCs and control groups.

4.2 MATERIAL AND METHODS

4.2.1 Participants

Eighty-two healthy older people participated in the study (40 men, 42 women). Participants were recruited in classes of La Nau Gran, a study program for people over 55 years old, and through advertisements on the campus of the University of Valencia (Spain).

The exclusion criteria were: history of alcohol or drug abuse; having had surgery under general anesthesia in the past year; uncorrected vision or hearing problems or any illness that involves an alteration of the nervous system and a neurologic or psychiatric disorder; and smoking more than 10 cigarettes a day. In addition, participants were excluded if they took drugs related to cognitive or emotional function, psychotropic 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.

All the participants completed the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), and three female participants who scored above 20 were excluded from the analysis. Therefore, the final sample was composed of 79 participants (all right-handed) who were distributed in two groups: SMCs (n = 41; 19 men and 22 women) and Control (n = 38; 21 men and 17 women). No significant differences in participants' age (t (77) = -1.010, p = .316), sex (χ^2 = 0.628, p = .428), or educational level (χ^2 = 7.063, p = .216) were observed between the SMC and Control groups (see Table 4.1).

Participants were distributed in these two groups according to their scores on the Spanish adaptation (Lozoya-Delgado et al., 2012) of the modified version of 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). We used these scores to distribute participants in the two conditions: participants who scored above 21 were allocated to the SMCs group, whereas participants who scored equal to or below 21 were included in the Control group. Twenty-one was the mean score obtained by the whole sample on the MFE-30 scale. Lozoya-Delgado et al. (2012) also observed that 21 was the mean score on this questionnaire in a sample of 900 Spanish participants. Notably, cut points and categorical distinctions are used in clinical practice and may be helpful to neuropsychologists using this questionnaire.

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

Table 4.1. Means (and standard deviations) for demographic data.

Demographic measures	SMCs (n = 41)	Control (n = 38)	Men (n = 40)	Women (n = 39)
Sex	19m/22w	21m/17w		
Age	63.9 (5.3)	65.24 (5.7)	65.43 (6.6)	63.72 (5.4)
Educational level				
Primary	5 (6.33%)	3 (3.8%)	3 (7.5%)	5 (12.8%)
Secondary	16 (20.25%)	8 (10.12 %)	10 (25%)	14 (35.9%)
University	20 (25.31%)	27 (34.1%)	27 (67.5%)	20 (51.2%)

Note. SMCs = subjective memory complaints; Control = no subjective memory complaints; m= men; w=women.

4.2.2 Procedure

Each participant attended two individual sessions on two consecutive days. Sessions lasted approximately two hours, either in the morning (between 10 and 12 am) or in the afternoon (between 15-17 or 17-19 pm). Half the participants attended in the morning and the other half in the afternoon. Each participant started both sessions at the same time of the day.

The first session consisted of a neuropsychological assessment, and the second session consisted of ERPs recording.

In each session, the experimenter checked whether participants had followed the instructions offered previously, which were: abstain from heavy physical activity the day before the session; do not consume alcohol or any stimulant since the night before the session; and sleep as long as usual. Moreover, participants were instructed to drink only water, and not eat, smoke, or take any stimulants such as coffee, cola, tea, or chocolate one hour before the experimental session.

4.2.2.1 Session one: neuropsychological assessment

In the first session, the weight and height of the participants were measured. In addition, they completed the MFE-30, the BDI-II, and a General Questionnaire with demographic data. Then, a neuropsychological evaluation was carried out. Participants performed four tests to measure EF domains, namely verbal working memory, visuo-spatial working memory, attention-switching, and verbal fluency.

Verbal working memory. It was evaluated with the Digit Span Test of the Wechsler Memory Scale (Wechsler, 1997). This test consists of two subtests that are administered independently: (a) the Digit Span Forward (DS-Forward), a measure of attention; and (b) the Digit Span Backward (DS-Backward), a measure of the executive component of working memory (Conklin et al., 2000). On the DS-Forward, the subject listens to numbers and has to repeat them in the same order. For the DS-Backward, the subject listens to numbers and has to repeat them in the reverse order. On this task, the sequences start at level 2 and can increase up to level 8. Subjects get two chances for each sequence length; if one of the sequences is performed correctly, the next sequence starts. Two measures were obtained: (a) DS-Forward:

total number of correctly recalled trials in the same order; and (b) DS-Backward: total number of correctly recalled trials in the reverse order.

Visuo-spatial working memory. The Automated Working Memory Assessment (AWMA) was used to assess visuo-spatial working memory (Alloway, 2008). On the Dot Matrix Forward subtest, the subjects point out the red dots in the same order they appeared. On the Dot Matrix Backward subtest, the subjects point out the boxes in the reverse order to the way they appeared. Two measures were obtained: (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 sequences start at level 2 and can increase up to level 8. Subjects get two chances for each sequence length; if one of the sequences is performed correctly, the next sequence starts.

Attention-switching. The Trail Making Test (TMT) was employed. It consists of two forms: the TMT-A and the TMT-B. The TMT-A was used to assess general psychomotor speed and attention, and the TMT-B was administered to measure the efficiency of attention-switching performance (Reitan, 1958), a component of EF. This test requires participants to connect a series of circles with a pen. On the TMT-A, the circles are numbered from 1 to 25, and participants must connect them in increasing order. The TMT-B contains circles numbered from 1 to 13 and circles lettered from A to L, and participants must connect the circles in order, alternating from a number to a letter. Two measures were obtained: (a) TMT-A: total time required to finish part A; and (b) TMT-B: total time required to finish part B (less time means better performance).

Verbal Fluency. To measure phonological fluency, that is, cognitive organization and ability to carry out an unusual word search, focal attention, sustained attention, and inhibition process, participants were asked to generate as many words as possible beginning with the letters F, A, and S in 60 seconds. In addition, to assess semantic fluency, participants were

asked to generate as many words as possible in the semantic category "Animals" in 60 seconds. Only correct answers were scored; intrusions, repeated attempts, and variations within the same species were not considered. Instructions for the two fluency tasks were given following the administration procedures provided in the Barcelona test (Peña-Casanova, 1991). The measure obtained was the number of correct words listed in each category.

4.2.2.2 Session two: Face Stimulus task with EEG recording

Twenty-four hours later, participants returned for the second session. The participants were prepared for the EEG recording after a 15 min habituation to the laboratory. Next, the Face Stimulus task was presented and lasted approximately 12 min, with simultaneous EEG recording.

Face Stimulus task. Stimuli were 204 facial expressions of emotions with positive, negative, and neutral valences. There were 68 photos for each valence, with male and female models in equal proportion. Photos were presented randomly to the participants. All photos were presented in a uniform size, grayscale, black background, and they were displayed at the center of a 24-inch size screen. All photos were extracted from the Karolinska KDEF database to generate emotional stimuli (Lundqvist et al., 1998).

The stimuli were presented in the following sequence: (1) a fixation mark (+) appeared for 1000 to 1300 ms; (2) the face was presented for 200 ms; and (3) a blank screen was displayed for 800 ms. The images were presented using the E-prime software (v2.0). Participants were instructed to press the 1 key if the facial expression was positive, 2 if it was negative, and 3 if it was neutral. The participants were seated 70 cm away from the screen in a dimly lit, sound attenuated room. The task started with a trial run with 12 stimuli. Participants received feedback after each of these 12 photos, showing whether it was right or wrong.

EEG recording and data analyses. The EEG signal was collected using an EEG cap (Easycap, Falk Minow, Munich, Germany) from a 29 channel system, in accordance with the

international 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), using a BrainAmp Standard amplifier system (Brain Products, Germany). The electrode AFz was used as the system ground, and electrodes were referenced to FCz. Vertical and horizontal electro-oculograms were captured by additional electrodes (VEOG-, VEOG+, HEOG-, HEOG+) placed around the eyes. The electrode-to-skin impedances were lowered using electrolyte gel (SUPER-VISC High Viscosity Electrolyte-Gel, EasyCap, Brain Products GmbH), and they were maintained below 5 kΩ before starting the recording. Data were re-referenced to a common average signal of 23 electrodes (Joyce & Rossion, 2005). The EEG and EOG were amplified and then passed through (0.1Hz - 30 Hz) a band-pass filter using an IIR filter (24 db/octave roll-off). Stimulus-locked epochs were extracted in a range from -200 to 1000 ms. Trials were then corrected to the mean voltage of the baseline (−200 to 0 ms). Epochs with EOG artifacts, including blinking or eye movement, as well as skin potentials, were corrected off-line using the algorithm by Gratton and Coles (Gratton et al., 1983). Epochs with incorrect responses were removed from averaging. The N170 component was measured at T6 and T5 within the time window of 130-200 ms. The P300 and LPP components were measured at Pz because it is the region where P300 and LPP achieve their maximum amplitude within the time window of 200-500 ms and the mean value of their amplitude within 400-700, respectively. Off-line EEG processing and analyses were performed with Brain Vision Analyzer System (Brain Products, Germany) software. In order to investigate behavioral performance on the face stimulus task, we also calculated average RT and accuracy.

4.2.3 Statistical Analyses

To investigate differences between groups (SMCs vs. Controls) and sex on demographic and neuropsychological data, Student´s *t*-tests and chi-squared, respectively, were performed.

Independent repeated-measures ANOVAs were performed on behavioral performance (RT and accuracy), as well as the latencies and amplitudes of the N170, P300, and LPP components. In these analyses, both *Group* (SMCs, Control) and *Sex* (men, women) were between-subject factors, and *Emotional Valence* (positive, negative, neutral) was the within-subject factor. For the N170 component, *Hemisphere* (left, right) was also included as an additional within-subject factor. The ANOVAs including the Sex of face of stimulus were described in supplementary material. In the case of violation of sphericity, Greenhouse-Geisser corrected values were reported. *Post hoc* comparisons were performed using Bonferroni correction.

In order to examine possible relations between EF performance and amplitudes of the N170 (average of left and right hemisphere), P300, and LPP components, we calculated the valence difference score by subtracting positive and negative faces from neutral faces. To test whether N170, P300, and LPP amplitudes of face valence were correlated with DS-Backward, Dot Matrix-Backward, and TMT-B, we calculated partial Pearson's correlations with DS-Forward, Dot Matrix-Forward, and TMT-A, respectively, as covariates. In addition, to test whether N170, P300, and LPP amplitudes were associated with verbal fluency, we performed bivariate Pearson's correlations.

To investigate the main research question (interaction between Group and Emotional valence), we estimated a sample size of 72 participants for a small to medium effect size (f = 0.175, alpha = 0.05 and power = 0.90) for this interaction. We recruited 82 participants to

anticipate possible missing data. The level of significance was set at α = .05, and SPSS 26.0 was used to perform the statistical analysis

4.3 RESULTS

4.3.1 Neuropsychological measures

Results indicated that scores on DS-Backward, *t(*76) = -2.688, *p* = .009, and Dot Matrix-Forward, *t* (76) = -2.841, *p* = .006, were lower in the SMCs group than in the Control group. No statistically significant differences were found on any other neuropsychological measures (all *p* > .097).

Descriptive data for the neuropsychological variables are summarized in Table 4.2.

Table 4.2. Means (and standard deviations) for neuropsychological data.

Neurophysiological measures	SMCs	Control	Men	Women
DS-Forward	5.88 (0.135)	6.05 (0.160)	5.87 (0.732)	6.05 (1.075)
DS-Backward	5.73 (0.119)	6.26 (0.163)	6.13 (0.951)	5.85 (0.875)
Dot Matrix	4.28 (0.130)	4.84 (0.144)	4.62 (0.935)	4.49 (0.914)
Backward Dot Matrix	4.23 (0.170)	4.45 (0.149)	4.21 (1.174)	4.46 (0.790)
TMT-A	47.59 (2.584)	46.63 (2.855)	43.83 (16.116)	50.51 (17.335)
TMT-B	96.46 (6.747)	82.74 (4.678)	82.45 (30.414)	97.46 (42.496)
Semantic fluency	20.41 (1.026)	23.05 (1.187)	40.55 (9.837)	40.51 (12.783)
Phonetic fluency	39.78 (1.845)	41.20 (1.759)	22.60 (6.376)	20.74 (7.594)

Note. SMCs = subjective memory complaints; Control = no subjective memory complaints; TMT: Trail Making Test.

4.3.2 Behavioral Performance

Results for RT and accuracy data are presented in Table 4.3. For RT, a main effect of *Group* was observed, $F(1,77) = 6.268$, $p = .014$, $\eta p^2 = .075$, indicating a longer RT in the SMCs group than in the Control group. A significant main effect was also observed for *Sex*, $F(1,74) = 5.201$, $p = .025$, $\eta p^2 = .066$), with men showing longer RT than women. Moreover, a significant effect of *Emotional Valence,* $F(1.799, 131.640) = 28.070$, $p = .001$, $\eta p^2 = .275$, was found. *Post hoc* comparisons showed that RT were longer for negative and neutral faces than for positive faces (both $p < .001$). No differences were found between negative and neutral ($p = .099$) faces. Interactions were not significant (all $p > .669$).

For accuracy, a significant effect of the *Group* factor $F(1, 74) = 4.680$, $p = .034$ $\eta p^2 = .059$) was found, with the SMCs group showing less accuracy than the Control group. We also found a significant effect of *Emotional Valence* $F(1.706, 126.261) = 81.677$, $p = .001$, $\eta p2 = .525$). Accuracy was better for positive faces than for negative and neutral faces (both $p = .001$), and better for neutral faces than for negative faces ($p = .001$). Neither the main effect of Sex ($p = .866$) nor any interaction reached statistical significance (all *ps* > 944).

Table 4.3. Means (and standard deviations) for behavioral performance by group and sex.

	SMCs	Controls	Men	Women
RT (ms)				
Positive	864.01 (106.50)	811.83 (89.02)	815.70 (109.11)	861.88 (103.62)
Negative	970.53 (106.06)	887.25 (174.48)	893.84 (179.19)	966.75 (99.79)
Neutral	948.80 (117.09)	891.82 (125.23)	893.72 (130.76)	948.36 (111.43)
Accuracy (%)				
Positive	89.7 (5.90)	94.02 (2.30)	92.3 (4.80)	92.22 (4.64)
Negative	72.0 (9.8)	76.4 (7.34)	73.19 (8.22)	74.82 (9.66)
Neutral	85.5 (7.44)	88.06 (7.10)	88.08 (6.28)	86.20 (8.18)

Notes. RT= reaction time; SMCs = subjective memory complaints; Controls = no subjective memory complaints.

4.3.3 ERP data analyses

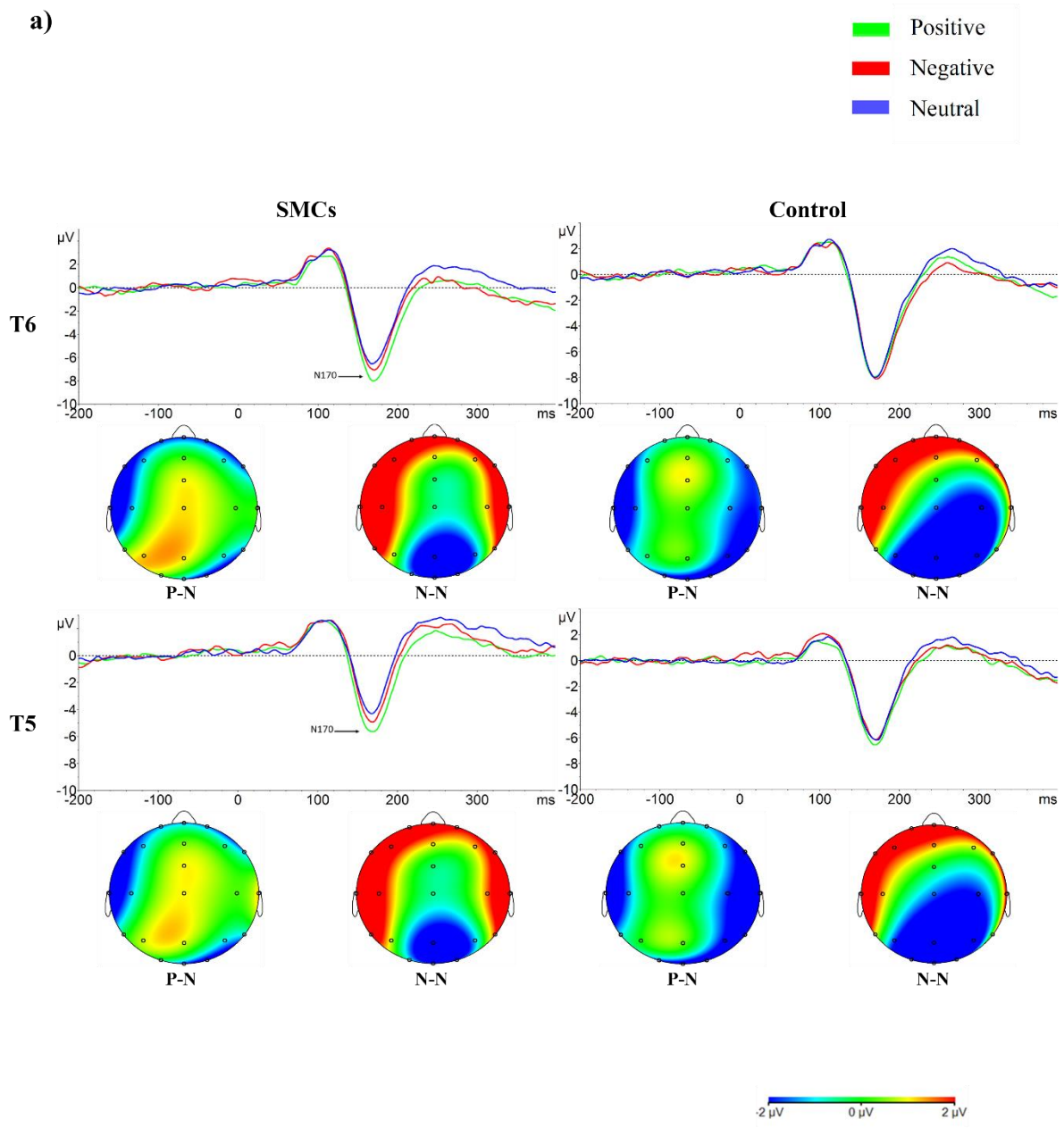
4.3.3.1 N170 component

For N170 latencies, the effect of *Emotional Valence* was significant, $F(2,138) = 8.462$, $p < .001=$, $np^2 = .109$, with longer N170 latencies for negative faces than for positive ($p = .001$) and neutral ($p = .005$) faces. Moreover, we observed a significant effect of Sex, $F(1, 69) = 6.396$, $p = .014$, $\eta p^2 = .085$, with men showing longer latencies than women. In addition, a significant interaction between Group*Sex, $F(1,69) = 4.389$, $p = .040$, $\eta p^2 = .060$, was found. *Post hoc* analyses revealed that men with SMCs showed longer latencies than women with SMCs ($p < .001$) (see Figure 4.1). We also found a significant Emotional Valence*Group*Sex interaction, $F(2, 138) = 3.379$, $p = .037$, $\eta p^2 = .047$. *Post hoc* analyses revealed that men in the SMCs group showed longer latencies than women in the SMCs group for negative ($p = .007$), positive ($p = .002$), and neutral ($p < .001$) faces. Furthermore, men with SMCs showed longer latencies than men in the control group for positive ($p = .016$) and neutral ($p = .005$) faces, but not for negative faces ($p = .114$). In addition, women with SMCs revealed longer latencies for positive ($p = .027$) and negative faces ($p = .002$) than for neutral faces (see Figures 4.1.a and 4.2). The remaining interactions were not significant (all $p > .806$) (see Figure 4.1).

For the N170 amplitudes, results showed a main effect of *Hemisphere*, $F(1,69) = 7.262$, $p = .009$, $np^2 = .095$, with higher amplitudes registered in the right hemisphere than in the left hemisphere. The Hemisphere*Sex interaction was also significant $F(1,69) = 4.671$, $p = .034$, $np^2 = .063$, with women eliciting higher amplitudes over the left hemisphere than men ($p = .043$). Other factor and interaction effects were not significant (all $p > .940$) (see Figure 4.1).

Figure 4.1. N170 latencies and amplitudes by groups and sex. (**a**) Grand average N170 for positive, negative, and neutral faces recorded in the right and left hemispheres in older people with and without subjective memory complaints. (**b**). Grand average N170 for positive, negative, and neutral faces recorded in the right and left hemispheres in men and women. Topographical distribution maps of the difference waves (P-N: positive vs. neutral and N-N: negative vs. neutral) are also shown in the time interval of 160-180 ms.

a)



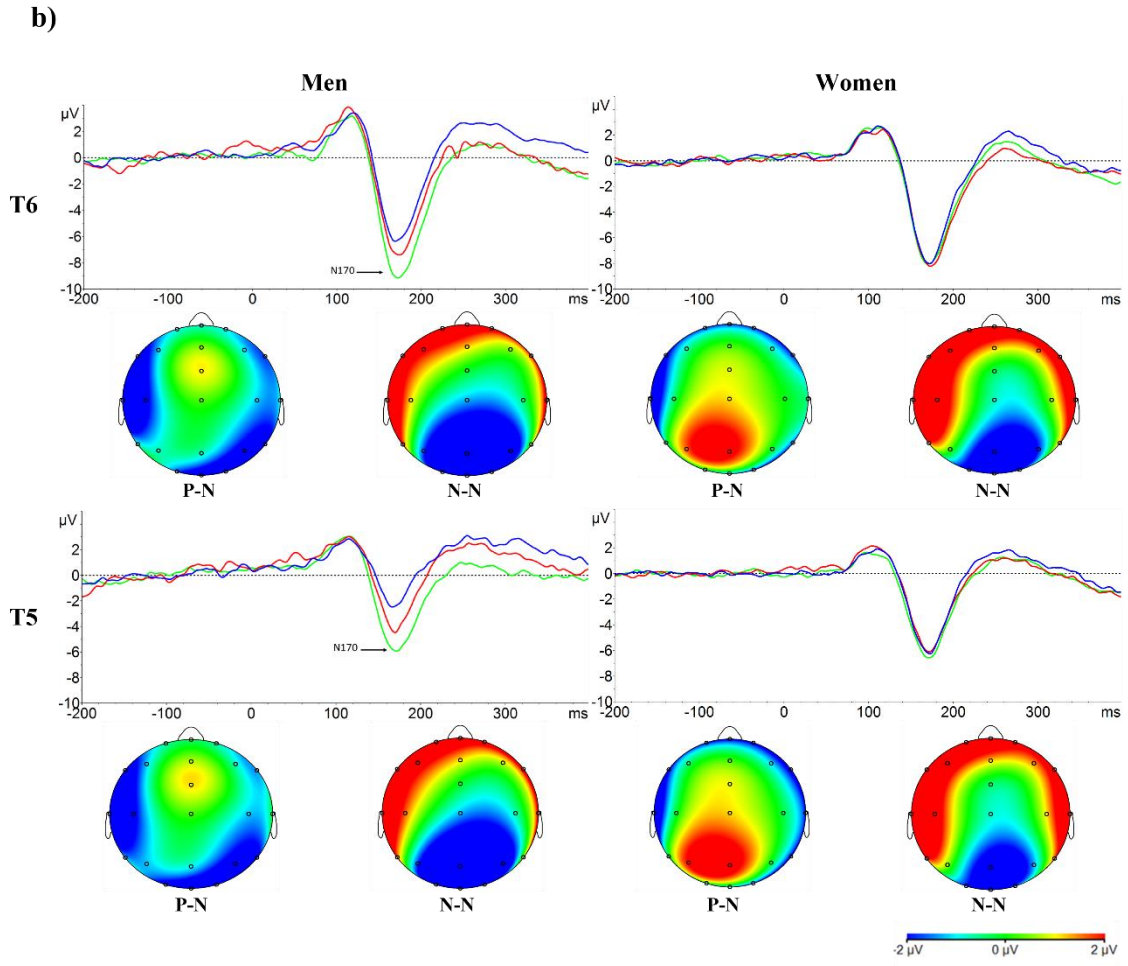
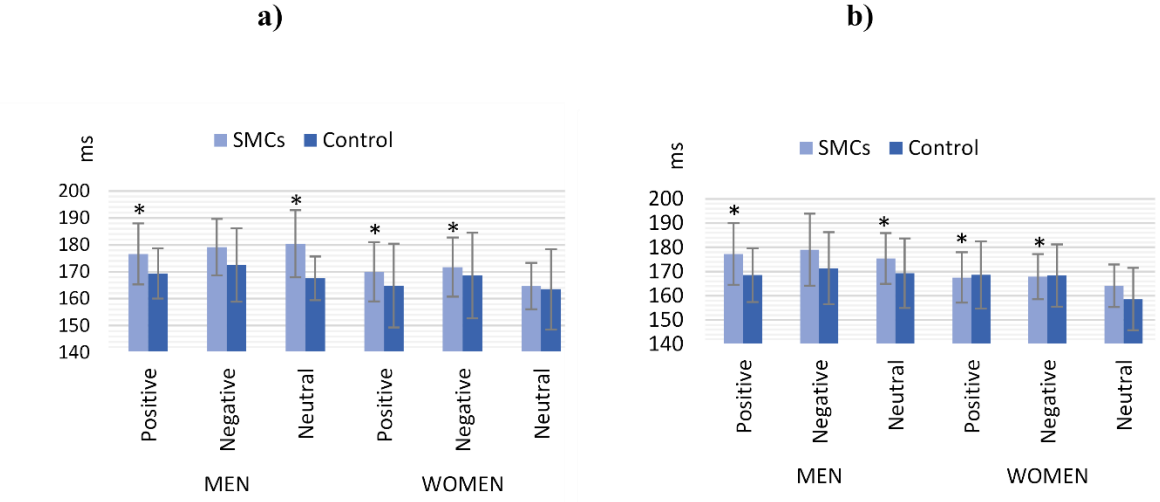


Figure 4.2. Mean latencies (ms) for the N170 component at the T6 electrode (a) and at the T5 electrode (b). Error bars indicate the standard error of the mean.



4.3.3.2 P300 component

For P300 latencies, the analyses indicated that the effects of *Emotional Valence*, *Group*, *Sex*, and their interactions were not significant (all $p > .876$) (see Figures 4.3 and 4.4).

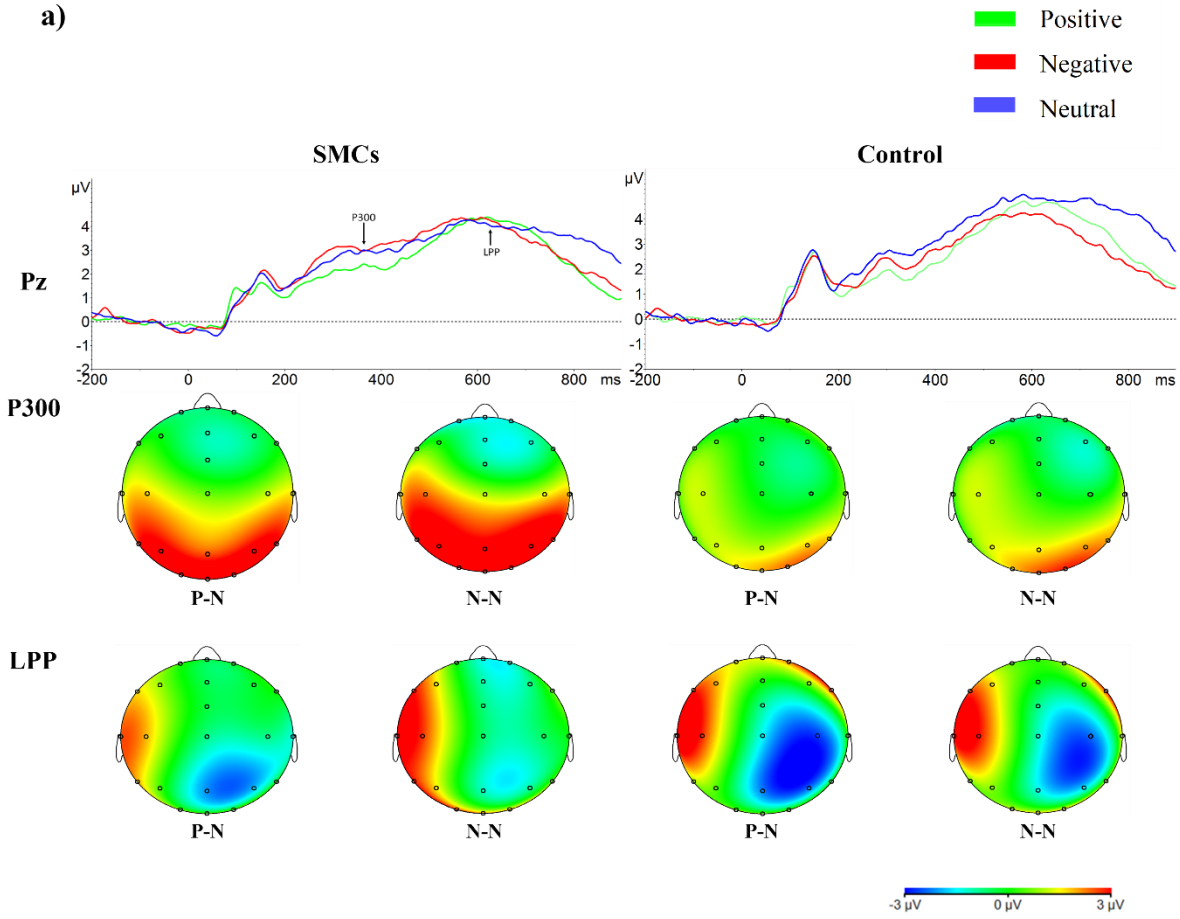
For P300 amplitudes, results showed a main effect of *Emotional Valence*, $F(2, 152) = 7.902$, $p = .001$, $\eta p^2 = .094$. *Post hoc* comparisons revealed that the amplitudes were significantly higher for negative faces than for positive faces ($p = .015$), and for neutral faces than for positive faces ($p = .002$), but not for negative and neutral ($p > 0.99$) faces. In addition, the *Sex* factor was significant, $F(1, 76) = 7.626$, $p = .007$, $\eta p^2 = .091$, with men showing smaller P300 amplitudes than women (see Figure 4.3.b). No other factor or interaction effect reached statistical significance (all $p > .591$) (see Figure 4.3).

1.1.1.1 LPP component

For LPP latencies, the analyses revealed that *Emotional Valence* was significant, $F(2, 198) = 6.528$, $p = .002$, $\eta p^2 = .118$. *Post hoc* comparisons showed longer latencies for positive faces than for neutral faces ($p = .008$), but no other significant differences were found (all $p > .746$). The main effects of *Group*, *Sex*, and other interactions were not significant (all $p > .933$) (see Figures 4.3 and 4.4).

For LPP amplitudes, the analyses indicated that *Emotional Valence, Group, Sex*, and their interactions were not significant (all $p > .941$) (see Figure 4.3).

Figure 4.3. P300 and LPP latencies and amplitudes by group and sex. (**a**). Grand average P300 for positive, negative, and neutral faces in older people with and without subjective memory complaints. (**b**). Grand average P300 for positive, negative, and neutral faces recorded in men and women. *$p < 0.05$. Topographical distribution maps of the difference waves (P-N: positive neutral and N-N: negative vs. neutral) are also shown in the time interval of 200-500 ms for P300 and time interval of 450-700 for LPP.



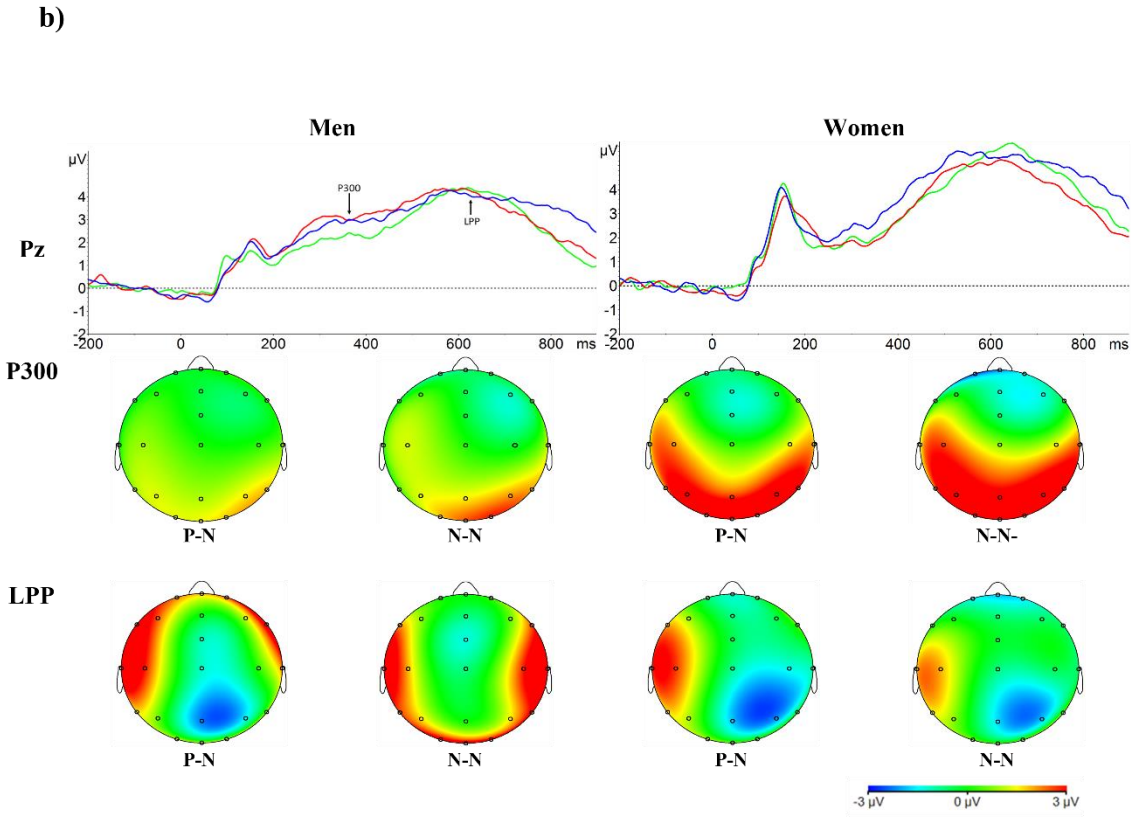
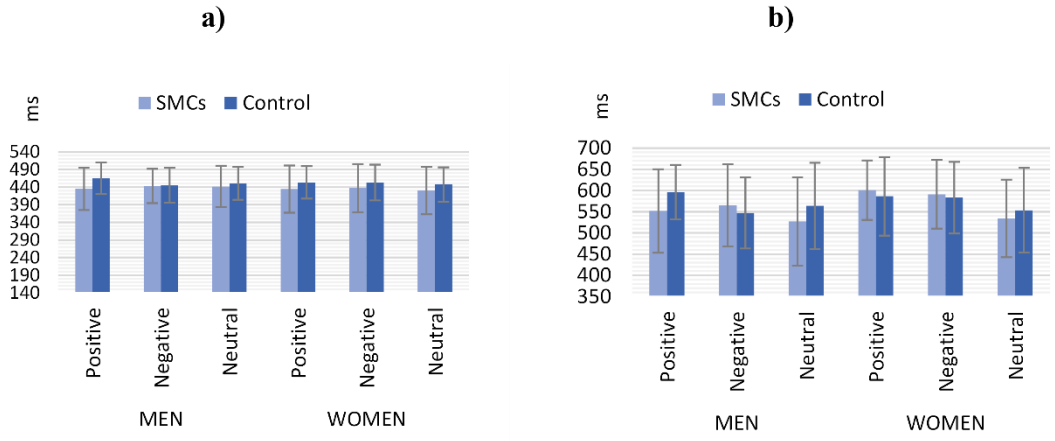


Figure 4.4. Mean latencies (ms) for the P300 component at the Pz electrodes (a) and for the LPP component at the Pz electrode (b). Error bars indicate the standard error of the mean.



1.1.2 Relationships between ERPs and EF performance

Table 4.4. shows the relationships between the P300, N170, and LPP amplitudes and EF performance. Because we are interested in emotion-related modulation, in the correlation analyses we used the difference score (negative vs. neutral and positive vs. neutral) for the amplitudes of the ERPs components. In the SMCs group, higher P300 amplitude for negative vs. neutral faces was correlated with better performance on DS-Backward (r = .367, p = .026) and Dot Matrix-Backward (r = .343, p = .035), and worse performance on TMT-B (r = -.375, p = .019). Moreover, a higher LPP amplitude for negative vs. neutral faces was associated with better performance on DS-Backward (r = .353, p = .035) and TMT-B (r = -.466, p = .003).

In the Control group, a higher P300 amplitude for negative vs. neutral faces was correlated with worse performance on Dot Matrix-Backward (r = -.349, p = .043). Moreover, a higher N170 amplitude for positive vs. neutral faces was correlated with worse performance on Dot Matrix-Backward (r = -.388, p = .023). In contrast, a higher N170 amplitude for negative vs. neutral faces was correlated with better performance on the same task (r = .396, p = .020).

Table 4.4. Correlations between N170, P300, and LPP amplitudes and executive function performance for SMCs and Control groups

Groups		Valences	DS-Backward	Dot Matrix-Backward	TMT B	Semantic fluency	Phonological fluency
SMCs	P300	P-N	*r* = -.028	*r* =.307	*r* =-.249	*r* =-.167	*r* =-.142
			p =.868	*p* =.061	*p* =.127	*p* =.304	*p* =.382
		N-N	***r* =.367**	***r* =.343**	***r* =-.375**	*r* =-.017	*r* =.043
			***p* =.026**	***p* =.035**	***p* =.019**	*p* =.919	*p* =.794
	N170	P-N	*r* =.035	*r* =.196	*r* =-.080	*r* =-.058	*r* =-.009
			p =.839	*p* =.238	*p* =.630	*p* =.720	*p* =.957
		N-N	*r* =.007	*r* =.232	*r* =-.275	*r* =.238	*r* =.096
			p =.967	*p* =.161	*p* =.091	*p* =139	*p* =.556
	LPP	P-N	*r* =.124	*r* =.234	*r* =-.248	*r* =-.160	*r* =-.237
			p =.473	*p* =.164	*p* =.134	*p* =.330	*p* =.146
		N-N	***r* =.353**	*r* =-.055	***r* =-.466**	*r* =.124	r =-.089
			***p* =.035**	*p* =.745	***p* =.003**	*p* =.451	*p* =.590
Control	P300	P-N	*r* =.164	*r* =0.188	*r* =-.100	*r* =.008	*r* =.283
			p =.354	*p* =0.287	*p* =.575	*p* =964	*p* =.100
		N-N	*r* =.321	***r* =-.349**	*r* =-.051	*r* =-.222	*r* =-.045
			p =.064	***p* =.043**	*p* =.775	*p* =.200	*p* =.799
	N170	P-N	*r* =-.132	***r* =-.388**	*r* =-.034	*r* =-.075	*r* =.181
			p =.458	***p* =.023**	*p* =.847	*p* =.670	*p* =.298
		N-N	*r* =-.235	***r* =.396**	*r* =-.120	*r* =.225	*r* =.133
			p =.181	***p* =.020**	*p* =.500	*p* =.194	*p* =.446
	LPP	P-N	*r* =.253	*r* =-.163	*r* =.148	*r* =-.076	*r* =.095
			p =.156	*p* =.365	*p* =.412	*p* =.667	*p* =.593
		N-N	*r* =.269	*r* =-.182	*r* =.101	*r* =-.125	*r* =.026
			p =.130	*p* =.310	*p* =.577	*p* =.483	*p* =.884

Notes. Significant partial correlations are displayed in bold. In correlation analyses we represent all correlations in italic and significant correlations in bold with italic. Abbreviations: Control, no subjective memory complaints; N-N, negative vs. neutral; P-N, positive vs. neutral; SMCs, subjective memory complaints; TMT, trail making test.

1.2 DISCUSSION

The main aim of the current study was to determine whether facial emotion processing was different in older people with and without SMCs by comparing behavioral and ERPs data. Summarizing the main findings, in agreement with the behavioral hypothesis, participants with SMCs had longer RT and less accuracy on facial emotional processing than participants without SMCs. In addition, we investigated whether SMCs participants showed longer latencies and smaller amplitudes in N170, P300, and LPP than participants without SMCs. In

this regard, ERPs analyses revealed group differences only in the N170 component. More specifically, men with SMCs showed longer latencies than men in the control group, and men with SMCs revealed longer latencies than women with SMCs. Moreover, women with SMCs showed longer latencies for positive and negative faces than for neutral faces. In contrast, we failed to find differences in P300 and LPP latencies and amplitudes between participants with and without SMCs. Furthermore, regarding the possible association between ERPs measures and EF performance, we found that higher amplitudes of P300 and LPP for negative vs. neutral faces were associated with higher levels of verbal and visuo-spatial working memory and general psychomotor speed and attention.

At the behavioral level, supporting our hypothesis, results showed that participants with SMCs performed worse than controls on the facial emotion processing task, reflected in longer RT and less accuracy. Our findings are similar to previous studies on facial emotion processing in people with MCI and AD (Pietsching et al., 2015; Teng et al., 2007; Varjassyová et al., 2013; Yang et al., 2015). Thus, this deficit in these patients may be an effect of progressive global cognitive degeneration (Pietsching et al., 2015; Spoletini et al., 2008) detected earlier.

Regarding the ERPs hypothesis, in the current study, on the one hand, we found that men with SMCs showed longer latencies than men in the control group for positive and neutral faces but not for negative faces. On the other hand, women with SMCs revealed longer latencies for positive and negative faces than for neutral faces. Additionally, men with SMCs also exhibited longer latencies for the three valences than women with SMCs. Although sex-specific differences in facial emotion processing have been previously reported in the general population (Herlitz & Loven, 2013), only one study has explored the role of sex in people with SMCs (Pietschnig et al., 2015). This study demonstrated a strong disadvantage for men with SMCs, compared to women, on a facial emotion recognition task, which could be consistent with our neural findings. Our results suggest that the difficulties in facial emotional processing

are experienced differently depending on the sex of the individual. In this vein, potential deficits in facial emotion processing in men with SMCs deserve attention. However, it is important to note that our study may be underpowered to detect more subtle sex-related differences. Therefore, more research is needed to investigate this idea.

The N170 component is considered an indicator of face structure encoding (Eimer, 2000), where the structural representation of the face is associated with semantic learning to form an internal representation of a human face (Sagiv & Bentin, 2001). Although the findings regarding the sensitivity of the N170 to facial expression are inconsistent (see review: Hinojosa et al., 2015), one study reported that the N170 component participates in the processing of facial expressions, especially the early processing of emotional valences (Qiu et al., 2017). Hence, prolonged N170 latencies indicate that face structure encoding and emotional processing may be slower in older people with SMCs. Similar results have been reported in people with MCI (Schefter et al., 2013; Yang et al., 2015). Interestingly, previous studies revealed that prolonged face structure encoding is associated with longer RT and has a negative correlation with accurately recognizing emotional faces (Schefter et al., 2013). Our behavioral data are consistent with this interpretation.

We did not find differences in P300 or LPP latencies or amplitudes in older people with and without SMCs. However, previous studies of P300 reported impairments in facial emotion processing in people with MCI and AD (Asaumi et al., 2014; Morgan et al., 2008). These mixed findings could be explained by methodological differences, such as the type of stimuli used, the difficulty of the task, or the severity of the participants' deficits. Additionally, these latter components (P300 and LPP) indicate an elaborate evaluation of emotional stimuli, and these components are susceptible to top-down processing, which involves sustained attention to visual emotional stimuli (Schupp et al., 2006). Our results indicate that later processing phases of emotional faces may be preserved in older people with SMCs.

Alternatively, the deficit in facial emotion processing might be associated with a decline in several executive functions. It has previously been proposed that facial emotion processing is interlinked with executive functioning (Ibáñez et al., 2011; Mathersul et al., 2009; Pessoa et al., 2009; Teng et al., 2007). In this regard, correlation analyses indicated that higher P300 and LPP amplitudes for negative vs. neutral faces were associated with working memory. P300 and LPP components increase their amplitudes for emotionally intense images (Schupp et al., 2006). From a biological perspective, negative faces have adaptive significance; however, in cognitive research, these increased amplitudes are associated with the meaning of task-relevant stimuli rather than their emotional significance (Olofsson et al., 2008; Schupp et al., 2006). Hence, the increased amplitudes found in the components would reflect a greater cognitive effort. Specifically, the LPP amplitude reflects the representation of stimuli in working memory. Thus, the working memory can also influence emotional processing because it maintains, stores, and updates facial features (Phillips et al., 2008). Therefore, top-down processes such as emotional evaluation appear to interact with working memory in the long-wave ERPs range.

Using other experimental paradigms, researchers reported a relationship between facial emotion processing and EF in older people with SMCs (Pietschning et al., 2015) and MCI (Teng et al., 2007). These authors suggest that poorer performance on EF tests may also serve as an index of generally increased degeneration in the frontal lobes, including the orbitofrontal regions, which may contribute to impairments in facial emotion processing (Teng et al., 2007). Likewise, the TMT-B (test sensitive to frontal lobe damage; Gouveia et al., 2007) correlated with the valence of the faces (negative vs neutral) in both components, P300 and LPP, suggesting that the processing of negative valences depends on executive functioning.

Regarding sex differences, our data indicate better performance by women than by men, regardless of the group, based on both the behavioral and ERPs (N170, P300, and LPP) data.

Our research supports and extends the evidence showing that women process affective information significantly better than men (Campanella et al., 2004; Choi et al., 2015; Li et al., 2008). This is consistent with the assumption that women show greater empathy, emotion recognition abilities, and interest in social information than men (Collignon et al., 2010; Lawrence et al., 2015; Proverbio, 2017).

Finally, in the behavioral data, on the one hand, the whole study sample was slower and less accurate on negative faces than on neutral and positive faces. This result is congruent with previous research (Carstensen et al., 2006; Mather & Carstensen et al., 2005; Ruffman et al., 2008), and it has been attributed to the positivity bias effect associated with aging, defined as a tendency for older people to attend better to positive emotional information than to negative and neutral emotional information (Mather & Carstensen et al., 2005; Ruffman et al., 2008). This age-related positivity effect could be attributed to an adaptive strategy to preserve emotion regulation and avoid social conflict (Carstensen et al., 2006; Ruffman et al., 2008). Another possible explanation may come from the theory of dynamic integration. This theory suggests that processing negative information is more cognitively demanding than processing positive information. Consequently, older people would process the latter better (Labouvie-Vief et al., 2003). On the other hand, in the whole sample, N170 amplitude elicited in the right hemisphere was higher than in the left hemisphere. This result emphasizes the role of the right hemisphere in face recognition tasks (Leleu et al., 2010), and it adds to a large body of evidence indicating increased N170 amplitude over the right hemisphere in response to emotional faces (Bentin et al., 1996; Luo et al., 2010).

A crucial strength of this study is the use of a reasonable sample of carefully selected participants. However, some limitations must be considered. Our participants had above-average education levels, which may not be representative of the population. Our stimuli only include stationary faces, which may not reflect the difficulties that older people with SMCs

might have in real life. Further studies using dynamic stimuli may offer a deeper understanding of emotional processing.

In conclusion, our results suggest that older people with SMCs show deficits in facial emotion processing that particularly affect early phases of face structure encoding and emotional valence processing. However, we failed to confirm deficits in the later and more complex stages of emotional processing in this population. Moreover, positive associations were observed between the P300 and LPP components and performance on tests of EF, suggesting that deficits in EF are likely to cause problems in facial emotion processing. These deficits could be due to the progressive degeneration of the brain structures modulating this process. These findings in this population can provide an opportunity to study deficits in emotional processing earlier in the degenerative process associated with MCI and AD.

CHAPTER 5.
EEG MARKERS AND SUBJECTIVE MEMORY COMPLAINTS IN YOUNG AND OLDER PEOPLE

The results of this chapter are under review in: Perez, V., Garrido-Chaves, R., Zapater-Fajarí, M., Pulopulos, M. M., Hidalgo, V., & Salvador, A. EEG markers and subjective memory complaints in young and older people. *International Journal of Psychophysiology*.

5.1 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 SMCs. SMCs have been conceptualized as subjective awareness of memory loss in the absence of any organic condition (Abdulrab & 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., 2015). 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 observed (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 & 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 & 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; Van 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 MCI or AD (Galluzzi & Frisoni, 2008).

The use of 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 (<1ms), which is ideal for studying the different frequency spectrums (Babiloni et al., 2016; Biasiucci et al., 2019). In this vein, EEG recording during resting conditions with EC and EO 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; 2020a). 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 EC and EO, 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).

5.2 MATERIAL AND METHODS

5.2.1 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 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 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 whole sample on the MFE-30 scale was 21. 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).

In both age groups, there were no differences between the SMCs and control groups in sex (χ^2 =.67, p = .443), educational level (χ^2 = .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 5.1.

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 more than 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.

Table 5.1. Means (and standard deviations) for demographic 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/m2)	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%)

Note. SMCs = subjective memory complaints; Control = no subjective memory complaints; m= men; w=women; BMI= body mass index; SES=subjective socioeconomic status.

5.2.2 Procedure

Each participant attended two individual sessions on two consecutive days. Sessions lasted approximately two hours 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 = 0.480) and young ($t_{(73)}$ =-0.446, p = 0.657) 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 two hours before the experimental session. Moreover, participants were instructed to drink only water.

5.2.2.1 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.

Verbal memory. It was assessed using the Spanish version of the FCSRT (Peña-Casanova et al., 1991), 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 seconds. After that, the free recall begins and lasts for 90 seconds. 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.

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) DS-Forward and 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.

Visuo-spatial working memory. To measure visuo-spatial working memory, the 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.

Attention-switching. The 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.

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 seconds. 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 x 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.

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).

5.2.2.2 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 Ohm. 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 three minutes during each of the EC and EO 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 three minutes (condition EO) and then closed their eyes for three minutes (condition EC). 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.

5.2.2.3 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., 2020b). 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 (EC, EO). Each three-minute epoch was divided into adjacent intervals of two seconds. 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. Density powers were 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.

5.2.3 Statistical Analyses

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 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* (EC and EO) served as within-subject factors. For EEG reactivity, 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.

Pearson´s correlations were performed to evaluate possible relationships between neuropsychological test scores and spectral power and EEG reactivity in each group (SMCs and control) and in each age group (older and young). To limit the number of variables, we performed an exploratory factor analysis with varimax rotation. Three factors were identified: (I) verbal memory, which explained 30.76% of the total variance; (II) EF, which explained 18.93%; and (III) attention, which explained 15.06% (total variance explained: 64.75%). The

Kaiser—Meyer—Olkin (KMO) indicated a satisfactory relationship between sample size and the number of variables (0.794), and Bartlett's test indicated that the correlations between variables were sufficient to warrant a factor analysis, C^2 (153) = 1063.656, p < 0.001. The verbal memory factor included: free recall on the first trials; total free recall; total recall; free delayed recall; and total delayed recall indexes from the FCSRT. EF was tested with the DS-Forward, DS-Backward, TMT-A Dot Matrix, Backward Dot Matrix, and Stroop Interference. Attention was tested with the TMT-B, Semantic fluency, phonetic fluency.

For the statistical analyses, the level of significance was taken as <0.05. SPSS 26.0 was used to perform the statistical analyses

5.3 RESULTS

5.3.1 Neuropsychological performance

In older people, results revealed that scores on free recall on the first trial ($t_{(65)}$ = -2.211, p = .031), and total recall ($t_{(65)}$ = -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).

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 = 0.005), and total delayed recall $t_{(70)}$ = -2.288, p = .035) on the FCSRT test were lower in SMCs than in the control group. However, considering the group means, it can be verified that both samples are within the normality 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 5.2.

Table 5.2. Means (and standard deviations) for neuropsychological data.

Neuropshycological measures	Older group		Young group	
	SMCs	Control	SMCs	Control
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 Interfenrence	-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; TMT: Trail Making Test.

5.3.2 Spectral power

In older people, the main effect of Frequency band, $F(2.324, 141.743) = 324.866$, $p < .001$, $\eta p2 = .045$, and Condition, $F(1, 61) = 42.144$, $p < .001$, $\eta p2 = .409$, as well as the Frequency Band*Condition*Group interaction, $F(2.744, 167.399) = 2.864$, $p = .043$, $\eta p2 = .045$, were statistically significant. Post hoc analyses revealed that older people with SMCs showed greater theta power in both the EO ($p = .034$) but no in EC ($p = .063$) conditions compared to controls (see Figure 5.1).

In young people, the main effects of Frequency band, $F(1.894, 132.592) = 471.177$, $p < .001$, $\eta p2 = .871$, and Condition, $F(1, 70) = 47.225$, $p < .001$, $\eta p2 = .403$, were significant. However, the Frequency Band*Condition*Group interaction was not significant, $F(2.398, 167.893) = 1.433$, $p = .240$, $\eta p2 = .020$ (see Figure 5.2).

Figure 5.1. 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)

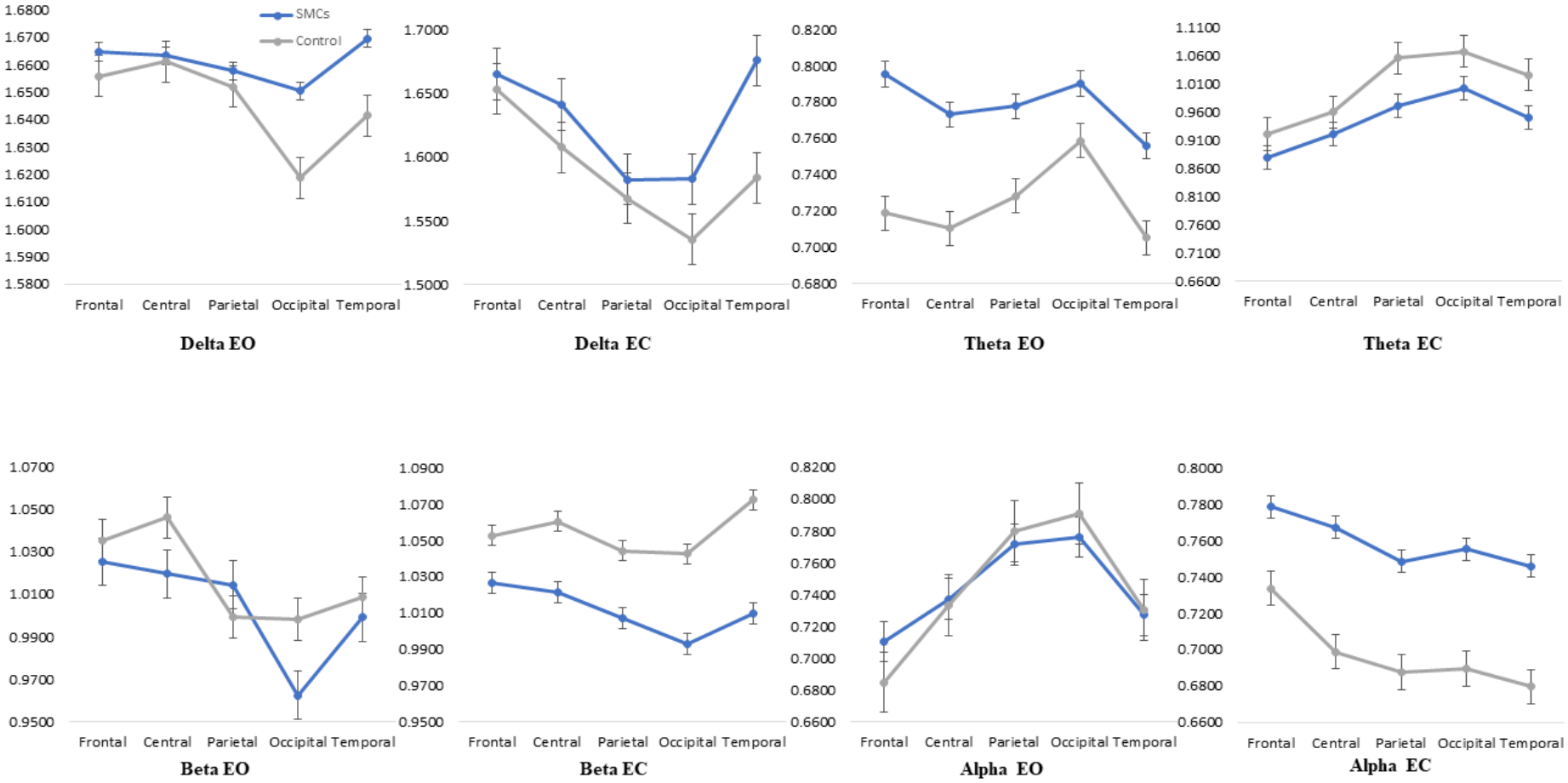
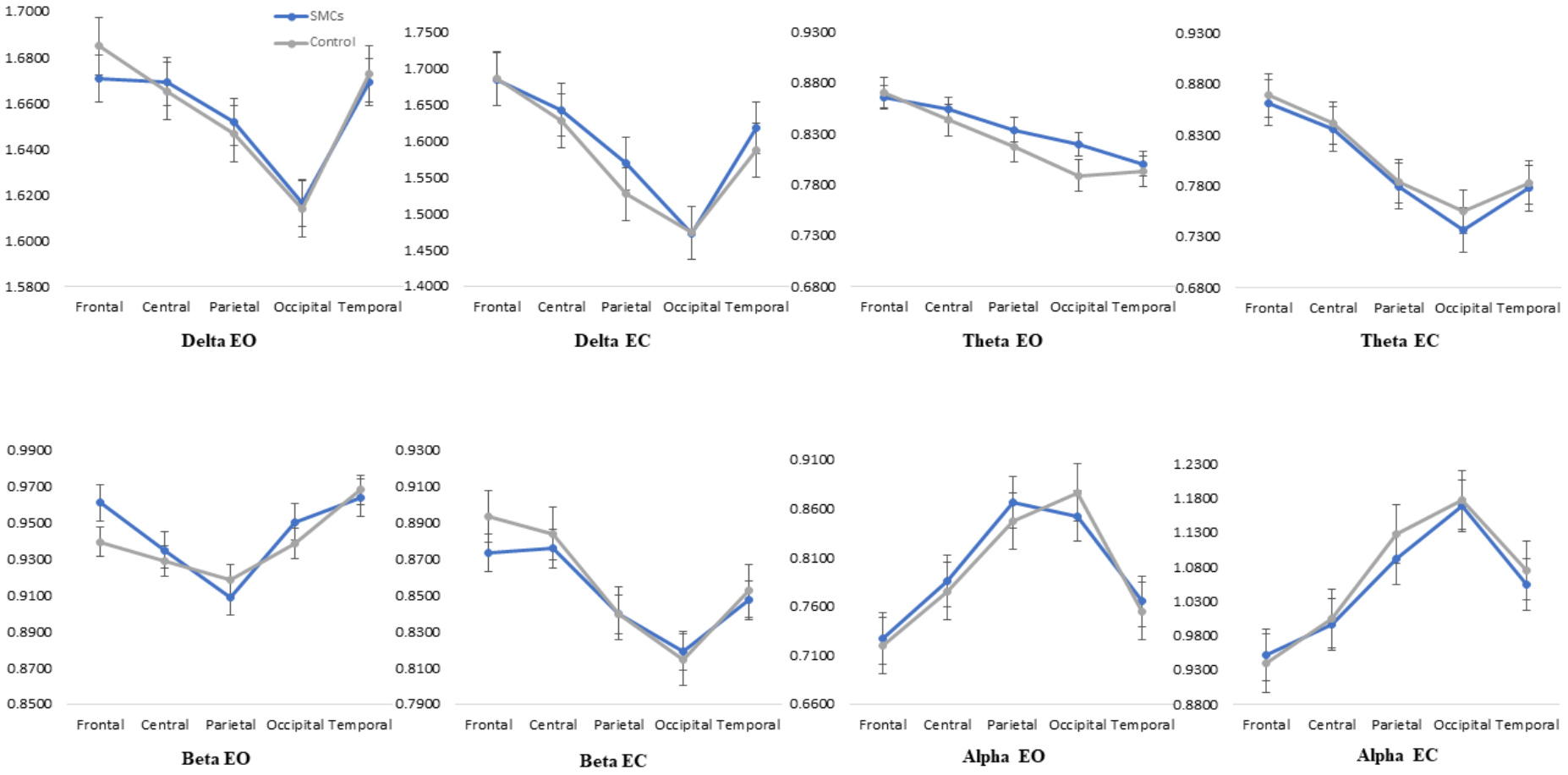


Figure 5.2. Means values and standard deviations of EEG spectral power analysis relative to the interaction effects among three factors: young groups (SMCs: subjective memory complaints and control), frequency bands (delta, theta, beta, alpha) and condition (EO: eyes open, EC: eyes closed)



5.3.3 EEG reactivity

In older people, the Frequency Band*ROI*Group interaction was significant, $F(12, 732) = 2.004$, $p = .022$, $\eta p2 = .032$. 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 $p = .505$).

5.3.4 Relationships between neuropsychological performance and spectral power

In older people with SMCs, in the EO condition, positive correlations were found between: factor (I) verbal memory and central theta power ($r = .365$, $p = .047$) and central ($r = .371$, $p = .034$), parietal ($r = .375$, $p = .032$), and temporal beta power ($r = .346$, $p = .049$). A positive correlation was also found between factor (III) attention and parietal delta power ($r = .363$, $p = .038$). In the EC condition, positive associations were found between: factor (I) verbal memory and occipital beta power ($r = .358$, $p = .041$); and factor (II) EF and frontal ($r = .357$, $p = .041$) and occipital beta power ($r = .415$, $p = .016$). Alpha bands and the rest of the ROI did not correlate significantly with any cognitive function in the EO and EC conditions for SMCs or control older people ($p > .959$).

Regarding EEG reactivity, in older people with SMCs, positive correlations were found between: factor (II) EF and EEG reactivity in frontal ($r = -.435$, $p = .011$), central ($r = -.508$, $p = .003$), and occipital beta ($r = -.470$, $p = .006$), and factor (III) attention and EEG reactivity in parietal delta ($r = .399$, $p = .022$). In the control group, a negative correlation was found between: factor (I) verbal memory and EEG reactivity in frontal

delta (r = -.337, p = .044). The rest of the bands and ROI did not correlate with any cognitive function (p > .992).

In young people with SMCs, in the EO condition, negative correlations were found between: factor (I) verbal memory and parietal theta power (r = -.359, p = .023); and factor (II) EF and central beta power (r = -.320, p = .044). In young control people, in the EC condition, factor (I) verbal memory was negatively correlated with temporal theta power (r = -.366, p = .031). Delta and alpha bands and the rest of the ROI did not correlate with any cognitive function in SMC and control young people (p > 971).

In addition, in young people with SMCs, negative correlations were found between: factor (I) verbal memory and EEG reactivity in frontal beta (r = -.316, p = .047); factor (II) EF and central beta (r = -.376, p = .017); and factor (III) attention and parietal (r = -.314, p = .048) and occipital beta (r = -.333, p = .036).

In the control group, positive correlations were found between: factor (II) EF and EEG reactivity in occipital theta (r = .346, p = .041); and factor (III) attention and EEG reactivity in temporal delta (r = .349, p = .040).

5.4 DISCUSSION

The present study aimed to determine 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 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 and beta spectral power were associated with better verbal memory, and higher delta spectral power was associated with better attention performance. In the EC condition, higher beta spectral power was associated with better verbal memory and EF performance. Likewise, higher beta and delta EEG reactivity were associated with better EF and attention performance, respectively. In young people with SMCs in the EO condition, lower theta spectral power was related to worse verbal memory. Similarly, lower beta spectral was associated with worse EF performance. Additionally, reduced beta EEG reactivity was related to worse verbal memory, EF, and attention performance.

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, 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, EF, 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 & MacLullich, 2006). This statement is supported by a prospective longitudinal study which reported that approximately 2.3% and 6.6% of older people with SMCs will progress to dementia and MCI per year (Mitchell et al., 2014). Moreover, several studies have observed neurophysiological changes in people with SMCs, such as smaller left hippocampal volume (Van 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).

Studies have shown that different degrees of hippocampal atrophy are correlated with an increase in theta power (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). The increased theta power revealed here in older people with SMCs confirms results from previous studies (Alexander et al., 2006; Gouw et al., 2017; Prichep et al., 1994). From a physiological viewpoint, EEG oscillations reflect the coupling of local groups of cortical inhibitory neurons and cortical excitatory pyramidal neurons (Biasiucci et al., 2019). Thus, less activation of these neurons due to a disruption in information processing in the cholinergic system may lead to an increase in theta power (Jeong, 2004; Roh et al., 2011).

In the present study, we also found changes in EEG reactivity. Older people with SMCs 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).

In older people with SMCs, spectral power increases in delta, theta, and beta were correlated with better performance on verbal memory, attention, and EF. Previous EEG studies carried out with this population have also shown an increase in delta power and better verbal/visuospatial memory and language production functions in MCI and AD patients (Babiloni et al., 2012), as well as an increase in theta power and better memory performance, including working and verbal memory (Alexander et al., 2006). The aforementioned cholinergic change at the theta power spectral might also affect the delta (Babiloni et al., 2012), which could result in less effectiveness on some cognitive measures. Regarding the theta band, 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). More intriguing is the correlation with beta frequency. Although beta activity has not been extensively studied in SMCs, it has been found to tend to decrease in neurodegenerative processes (Lejko et al., 2020), with the loss of relative power being more prominent in central and parietal regions (Prichep et al., 1994). Our results on this correlation contradict this statement, perhaps reflecting an initial compensatory processing. It has also been shown that the cholinergic system determines the compensatory response during early cognitive deterioration (Babiloni et

al., 2012). This hypothesis has previously been proposed to explain similar results in AD, where there was increased activation in people at risk of developing AD (Gaubert et al., 2019). According to these authors, a sufficient level of compensation is needed to maintain normal cognitive functioning in preclinical AD (Gaubert et al., 2019). Moreover, the higher beta and delta EEG reactivity associated with EF and attention performance might be related in some way to the mobilization of greater resources that ensure cognitive functioning and the reorganization of cortical networks in areas prone to age-related physiological changes (Barry & De Blasio, 2017).

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. Despite this lack of effects, in the correlation analyses, an opposite effect was observed compared to older groups. That is, increased spectral power in theta and beta was related to poor verbal memory and EF performance, and reduced beta EEG reactivity was related to worse verbal memory, EF, and attention performance. Young people with SMCs also performed worse than controls on verbal memory, supporting findings showing that changes in EEG activity could predict deficits on some neuropsychological tasks. These findings suggest that EEG changes may be nonlinear across young and older people with SMCs.

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. However, at the same time, many correlation analyses were performed, and the possibility of type I error cannot be ruled

out. Despite this limitation, this study benefits from a complete assessment of neurocognitive function that objectively establishes the absence of deterioration in SMCs.

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.

CHAPTER 6.
ALPHA PEAK PARAMETERS AND THEIR RELATIONSHIP WITH COGNITIVE RESERVE IN PEOPLE WITH SUBJECTIVE MEMORY COMPLAINTS

The results of this chapter are in preparation: Perez, V., Garrido-Chaves, R., Zapater-Fajarí, M., Hidalgo, V., & Salvador, A. Alpha peak parameters and their relationship with cognitive reserve in people with subjective memory complaints.

6.1 INTRODUCTION

SMCs may be valuable as a predictor of MCI or AD in older people (Abdulrab & Heun, 2008). SMCs are commonly reported with advancing age (Schütz et al., 2020) in the absence of any organic or identifiable condition known to produce memory disorders (Abdulrab & Heun, 2008). Although some studies have investigated the association between SMCs and objective memory performance in older and young people, the results have been inconsistent because not all complainers present deficits on objective cognitive assessments (Montenegro et al., 2013; Zlatar et al., 2018). This lack of association has led to examining whether people with greater CR might have more accessible resources with which to deal with cognitive decline over time (Lojo-Seoane et al., 2018). Therefore, CR is used to explain why two people with the same condition may have different clinical manifestations or cognitive performance (Stern, 2012). CR is defined as an active process through which the brain adapts to a deteriorating situation by using cognitive processing resources to compensate for deficits (Stern, 2009). Thus, knowledge about the impact of CR in people with SMCs could be used to develop successful and accurate diagnostic methods, given that high CR can mask the symptoms of cognitive impairment (Lojo-Seoane et al., 2014).

Similarly, knowledge about the underlying neurophysiological mechanisms could also contribute to understanding SMCs. In this vein, EEG is a non-invasive technique used to investigate the neural electrophysiological parameters of brain activity. EEG can detect ionic currents generated by postsynaptic activity in cortical neuron populations (pyramidal cells organized by cortical columns; Biasiucci et al., 2019). This postsynaptic activity occurs in standard frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (>30 Hz), and it can be recorded with resting EEG, which is commonly acquired during EC and/or EO conditions (Barry & De Blasio, 2017).

The anchor point for analysis of the EEG is the alpha rhythm, which dominates the EEG power spectrum in normal resting people (Klimesch, 1999). It has been argued that using the APF, defined as the frequency that shows its power peak within the extended alpha range, gives a more precise estimate of alpha modulated activity (Klimesch, 1999). APF is reported to exhibit characteristics of a stable marker of a neurophysiological trait (Klimesch, 1999) and show high heritability (Grandy et al., 2013a). Furthermore, APF changes with age, increasing up to middle age and then decreasing with older age (Aurlien et al., 2004). Additionally, there is a body of evidence showing that APF is positively linked to several cognitive functions such as memory, speed of information processing, timing of neural inhibition, and reading comprehension (Grandy et al., 2013a; Grandy et al., 2013b; Rathee et al., 2020).

The importance of APF in defining neurophysiological characteristics of dementia-related disorders has hardly been investigated. In a study following a cohort of MCI patients, alpha peak parameters (APF and amplitude) were found to be slower and reduced, respectively, compared to healthy controls, in posterior brain regions (Garcés et al., 2013). Likewise, APF was also lower in AD in comparison with MCI and healthy controls (Ruiz-Gómez et al., 2018).

In the SMCs literature, less attention has been paid to APF. Therefore, this study was conducted to investigate the alpha peak parameters, APF and amplitude, in people with SMCs and control people. We asked whether these parameters would not only differentiate between SMCs and controls, but also older and young people. Based on the literature summarized previously on MCI and AD, we hypothesized that older people with SMCs would also show lower APF and reduced amplitude compared to matched controls (Garcés et al., 2013; Ruiz-Gómez et al., 2018). Additionally, we hypothesized

that, in the context of age-related physiological differences, alpha peak parameters might be slowed down, as reported in a previous study (Scally et al., 2018).

Moreover, we analyzed whether this parameter was modulated by sex. Sex-linked differences in APF have also been reported. A study that utilized a clinical database found that women, from infancy to the late 80s, had higher APF than men (Aurlien et al., 2004). In addition, Ghazi et al. (2021) examined sex-related differences in APF while participants performed a working memory task, and they found that women showed more APF than men. Despite this evidence, to the best of our knowledge, possible sex-related differences in people with SMCs have not yet been determined. Therefore, we included both women and men in order to explore possible sex-related differences in older and young people with and without SMCs.

Finally, as far as we are aware, the relationship between CR and APF and amplitude has not been studied to date. Given the importance of SMCs in disorders related to dementia and the fact that CR has shown protective effects against cognitive impairment (Lojo-Seoane et al., 2018), we examine whether the alpha peak parameters are associated with CR in the context of SMCs in each age group (older and young).

6.2 MATERIAL AND METHODS

6.2.1 Participants

For this study, the sample recruited consisted of 165 participants divided into two age groups: 82 older adults and 83 young adults. Twelve older participants and eight young participants were excluded due to technical problems with their EEG records.

Consequently, the final sample employed was composed of 70 older adults (36 men, 34 women) and 75 young people (38 men, 37 women), all right-handed. The older people were recruited from La Nau Gran, a study program of the University of Valencia 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).

Participants were distributed into two groups according to their score on the Spanish adaptation of the MFE-30 (Lozoya-Delgado et al., 2012) (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. Therefore, participants scoring 21 or over comprised the SMC group, and participants scoring less than 21 were included in the Control group. In addition, Lozoya-Delgado et al. (2012) observed that 21 was the mean score on this questionnaire in a sample of 900 Spanish participants. Cut-off points and categorical distinctions are used in clinical procedures and may be helpful to neuropsychologists using this questionnaire.

Regarding older people, there were no differences in sex ($\chi2 = .68$, $p = .156$), age (t (68) = -.525, $p = .132$), SES (t (68) = -.921, $p = .360$), measured with the MacArthur Scale of Subjective Social Status (Adler et al., 2000), BMI (t (088) = .68, $p = .759$), CR (t (68) = -.702, $p = .093$), or educational level ($\chi2 = .6$, $p = .156$) between the SMCs and Control groups.

Regarding young people, no differences between the SMCs and Control groups were found in sex ($\chi2 = .1$, $p = .558$), age (t (73) = -1.869, $p = .066$), SES (t (73) = -.408,

p = .68), BMI (*t* (73) = -.217, *p* = .828), CR (*t* (73) = -1.118, *p* = .267), or educational level ($\chi 2$ = .6, *p* = .817).

Finally, no age differences were found in sex ($\chi 2$ = .1, *p* = .124), SES (*t* (151) = -1.443, *p* = .148), or CR (*t* (151) = -1.905, *p* = .059). However, older people had a higher BMI (*t* (151) = -6.132, *p* > 001) and educational level ($\chi 2$ = 2, *p* = .002) than young people. Descriptive data for demographic measures are summarized in Table 6.1.

Table 6.1. Means (and standard deviations) for demographic data

	Older People				Young People			
Demographic measures	SMCs (n=35)	Control (n=35)	Men (n=36)	Women (n=34)	SMCs (n=40)	Control (n=35)	Men (n=38)	Women (n=37)
Sex (men/women)	15m/20w	21m/14w			19m/21w	19m/16w		
Age	63.8 (5.6)	65.8 (5.2)	65.9 (1.6)	63.5 (5.2)	21.3 (3.3)	22.8 (3.7)	22.6 (3.7)	21.3 (3.4)
SES	5.9 (1.5)	6.3 (1.6)	6.2 (1.6)	5.8 (1.5)	5.7 (1.2)	5.8 (1.1)	6 (1.1)	5.6 (1.1)
BMI	26.0 (5.4)	26.4 (3.7)	28.3 (3.8)	24.1 (4.6)	24.1 (4.8)	24.6 (3.9)	22.8 (3.4)	21.9 (3.3)
CR	14.8 (3.9)	16.2 (2.8)	15.6 (2.9)	15.3 (3.9)	14.4 (3.4)	15.5 (2.3)	14.3 (2.8)	14.6 (3.2)
Educational level								
Primary	4 (5.5%)	3 (4.5%)	3 (4%)	4 (6%)				
Secondary	14 (20%)	8 (11.5 %)	9 (12.5%)	13 (19.5%)	33 (44%)	18 (24%)	24 (32%)	27 (36%)
University	17 (24.5%)	24 (34%)	24 (34%)	17 (24%)	9 (12%)	15 (20%)	14 (18%)	10 (14%)

Note. SMCs = subjective memory complaints; Control = no subjective memory complaints; m= men; w=women; SES=subjective socioeconomic status; BMI= body mass index; CR= cognitive reserve.

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 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 at 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.

6.2.2 Procedure

Participants were tested individually. The session lasted approximately two hours, 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).

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; refrain from consuming alcohol or any stimulant (i.e., caffeine, alcohol, cola, tea, or chocolate); and refrain from eating or

smoking for at least two hours before the session. Moreover, participants were instructed to drink only water.

6.2.2.1 Cognitive Reserve (CR)

To measure the CR, the Cognitive Reserve Questionnaire (Rami et al., 2011) was used. It includes eight items that measure various aspects of intellectual activity, such as: education, completion of training courses, parents' educational level, the occupation carried out throughout life, musical training, and knowledge of languages. In addition, it investigates the approximate frequency of cognitively stimulating activities related to lifestyle, such as reading habits and the practice of intellectual games. The maximum score is 25; the higher score, the higher the cognitive reserve. A score of 6 or less is considered the lowest cognitive reserve.

6.2.2.2 Resting state EEG recording

EEG was recorded using an EEG cap (Easycap, Falk Minow, Munich, Germany) from 29 electrode leads according to the international 10-20 electrode 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), using a BrainAmp Standard amplifier system (Brain Products GmbH, Germany). We removed the two mastoid electrodes because they contained low-quality EEG in many participants. Ground was placed at Fpz. 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 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. The EEG was recorded with a bandpass filter of 0.3-100 Hz and digitized with a sampling rate of 500 Hz. In addition, blink artifacts in

the rest condition were removed by Independent Component Analysis. After, segments were visually inspected, all the segments containing artifacts other than eye blinks and eye movements were removed from the data. All data were digitized in continuous recording mode for three minutes during each EC condition. Artifact corrected data were then subjected to a Fast Fourier Transform (FFT) using a Hanning window and zero padding to 10 s, in order to obtain a frequency resolution of 0.1 Hz.

EEG resting state data were acquired from three minutes of recording with EC in a quiet and softly lit room. Instructions for EEG recording encouraged participants to sit quietly, with relaxed muscles, no voluntary movement, and no talking. An experimenter monitored the EEG traces in real time and verbally informed the participants whenever there were signs of behavioral or EEG drowsiness.

6.2.3 Estimation of APF and Alpha amplitude

APF was estimated as alpha peak frequency from the mean spectrum over six posterior electrodes (Pz, P4, P3, Oz, O2, O1) by means of peak detection between 8 and 12 Hz (Fig 6.1). APF was computed for each participant involved in the study. Because the amplitude of alpha oscillations has also repeatedly demonstrated high stability in the presence of large inter-individual differences (Grandy et al., 2013b), we also performed stability analyses on estimates of alpha amplitude. Alpha amplitude was defined as the mean amplitude of the six posterior electrodes.

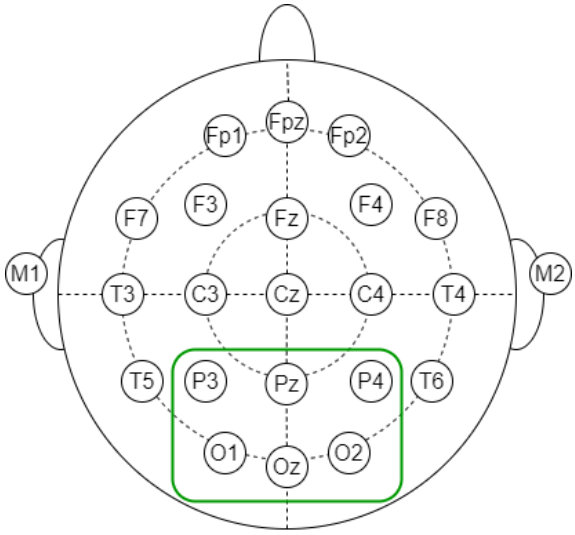


Figure 6.1. Six scalp posterior electrodes (green region) used to study the alpha parameter (alpha peak frequency and amplitude), positioned according to the International 10-20 System.

6.2.4 Statistical Analyses

Condition and age differences in the demographic data were analyzed using t-tests or $\chi 2$. APF values were analyzed using univariant analyses of variance (ANOVA), with APF as dependent variable and Condition (SMCs/control), Group (older/young), and Sex (men/women) as between-subject factors. For amplitude, a repeated-measures ANOVA was used, including Electrode (Pz, P4, P3, Oz, O2, and O1) as within-subject factor and Condition, Group, and Sex as between-subject factors. In the case of violation of sphericity, Greenhouse-Geisser corrected values were reported. *Post hoc* comparisons were performed using Bonferroni correction.

Pearson´s correlations were used to evaluate possible significant alpha peak parameters (APF and alpha amplitude) and CR relationships in each condition and group. We considered the Condition and Group in the correlation because these alpha peak parameters may be an interesting marker to test the effect of CR on SMCs in each age group.

For the statistical analyses, the level of significance was taken as <0.05. SPSS 26.0 was used to perform the statistical analysis.

6.3 RESULTS

6.3.1 APF

The analyses revealed that the Condition ($F(1,116) = .397$, $p = .530$, $\eta p^2 = 0.003$), Group ($F(1,116) = 3.311$, $p = .071$, $\eta p^2 = 0.028$), and Sex, ($F(1,116) = 2.129$, $p = .147$, $\eta p^2 = 0.018$), factors were not significant. In addition, the Condition*Group ($F(1,116) = .021$, $p = .884$, $\eta p^2 = 0.001$), Condition*Sex ($F(1,116) = .396$, $p = .531$, $\eta p^2 = 0.003$), Group*Sex ($F(1,116) = .165$, $p = .685$, $\eta p^2 = 0.001$), and Condition*Group*Sex($F(1,116) = .035$, $p = .852$, $\eta p^2 = 0.001$) interactions were not significant either (Fig 6.2).

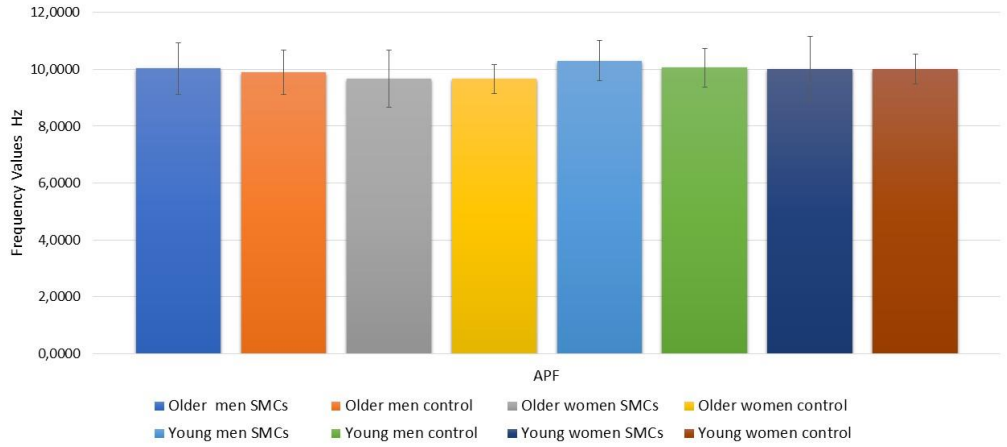


Figure 6.2. Mean and standard error of alpha peak frequency (APF) induced by conditions, subjective memory complaints (SMCs) and control, sex, and group.

6.3.2 Alpha amplitude

Results showed a main effect of Group ($F(1, 116) = 7.624$, $p = .007$, $\eta p2 = .062$), with young people eliciting higher amplitudes than older people. However, Condition ($F(1,116) = .238$, $p =$

.627, $\eta p^2 = 0.002$) and Sex ($F(1,116) = 2.123$, $p = .148$, $\eta p^2 = 0.018$), were not significant. In addition, the Electrode factor was significant ($F(5, 580) = 1.821$, $p < .001$, $\eta p2 = .116$), as was the Electrode*Group interaction ($F(5, 580) = 9.119$, $p < .001$, $\eta p2 = .073$). *Post hoc* comparison revealed that young participants showed higher amplitudes at O2 ($p = .001$), Oz ($p = .042$) and O1 ($p = .008$) than older people. No other significant differences were found (all $p > .763$). None of the other interactions reached statistical significance ($ps > 0.910$).

6.3.3 Correlations between APF, alpha amplitude and CR

Pearson's correlations indicated that APF was negatively correlated with CR in older people with SMCs, ($r = - .449$, $p = .029$), but no relationships between these two variables were found in older control people, young people with SMCs, or controls (all $p > .398$) (Table 6.2).

Regarding the association between alpha amplitude and CR, only in young control people, a positive correlation was found in Pz ($r = .376$, $p = .034$), P3 ($r = .438$, $p = .012$), and O2 ($r = .433$, $p = .013$). No other associations were observed (all $p > .963$) (Table 6.2).

Table 6.2. Correlations between APF and Pz, P4, P3, O2, O1, Oz amplitudes and CR in older and young people with SMCs and Control groups

	Older group		Young group	
	SMCs	Control	SMCs	Control
	CR			
APF	**r = -.449, *p*= .028**	r = -.187, *p*= .371	r = .143, *p*= .398	r = -.172, *p*= .338
Pz	r = -.156, *p*= .468	r = -.116, *p*= .580	r = -.202, *p*= .224	**r = .376, *p*= .034**
P4	r = -.010, *p*= .963	r = -.136, *p*= .517	r = -.165, *p*= .323	r = .309, *p*= .085
P3	r = .056, *p*= .796	r = -.164, *p*= .434	r = -.169, *p*= .310	**r = .438, *p*= .012**
O2	r = .149, *p*= .489	r = -.223, *p*= .285	r = -.092, *p*= .582	**r = .433, *p*= .013**
O1	r = .248, *p*= .243	r = -.201, *p*= .336	r = -.024, *p*= .888	r =. 341, *p*= .056
Oz	r = -.109, *p*= .612	r = -.136, *p*= .518	r = -.039, *p*= .814	r = 301, *p*= .094

Note. SMCs = subjective memory complaints; Control = no subjective memory complaints; CR = Cognitive Reserve; APF = alpha peak frequency. Significant partial correlations are displayed in bold.

6.4 DISCUSSION

In this study, the alpha peak parameters (APF and alpha amplitude) were investigated in a sample of people with SMCs and controls, considering the influence of age and sex. In addition, in each condition and group, correlation analyses between the two alpha peak parameters and CR were performed. Summarizing the main findings, no condition or sex differences were found in the two alpha peak parameters. However, we reproduced the previous findings detecting a reduced amplitude in older people compared to young adults. Finally, the results showed that, in older people with SMCs, a high CR was associated with slowing APF. By contrast, in young people in the control group, a high CR was correlated with greater Pz, P3, and O2 amplitudes.

No significant differences between conditions (SMCs and control) were found in APF and alpha amplitudes. Thus, the hypothesis that the alpha peak parameters in SMCs are slower when compared with a control population could not be confirmed in our sample. This lack of effect contrasts with previous studies that reported a slower mean APF and decreased amplitude in MCI (Garcés et al., 2013) and a reduced mean APF in AD (Ruiz-Gómez et al., 2018). This slowing in peak frequency found in neurodegenerative disorders might be explained by a redistribution of the oscillatory sources in the theta-alpha frequency range (Garcés et al., 2013). Even though SMCs have been considered a prodromal form of MCI and AD, we failed to find differences compared to controls. One might assume that the lack of significant differences between SMCs and control people in our study was due to the fact that APF is highly stable within individuals in the absence of pathology (Grandy et al., 2013b). Likewise, the alpha amplitude was shown to be stable between conditions. The amplitude of alpha oscillations, as in APF, has also been shown to be highly reliable and stable in the presence of large inter-individual differences (Grandy et al., 2013b). Another possible explanation for the lack of

differences between groups might be the age of the participants, given that the average age of previous study samples was >10 years older than the present sample.

In addition, the APF and amplitude also depend on factors such as age or sex. In our study, older and young adults had similar APF, with older people showing only a 0.12 Hz difference compared to young people. Klimesch (1999) postulated that APF remains stable during adulthood and then starts to decrease with age. Despite this, in a life-span study, Aurlien et al. (2004) described a steady decline in APF from birth to age 30, when APF stabilized for the rest of the lifespan. This would explain the fact that the healthy young and older people in this study have a similar APF. In fact, the mean frequencies of our sample agree with reported averages in young adults (age 17-30), which range from 9.8-10.5 Hz to 8.5-9.7 in older adults aged 60 and above (Aurlien et al., 2004). In contrast, amplitudes were significantly reduced in older people, especially in the occipital regions, as has been well documented in previous studies (Scally et al., 2018), leading to the conclusion that, although no slowing of APF was seen, alpha production might be compromised in older people. Using magnetic resonance imaging, age-related structural changes in the thalamus have been observed (Cherubini et al., 2009) and may, therefore, be expressed in the EEG through attenuation of the alpha amplitude. Further neuroimaging work is needed to disentangle these relationships.

Regarding sex, one study conducted in MCI showed higher APF in women than in men (Garcés et al., 2013). This trend is maintained in healthy people (Chiang et al., 2011). However, in our study, we report similar APF and amplitudes between sexes and between conditions. Note that the sample used in the study by Chiang et al. (2011) comprises subjects ranging from 6 to 86 years of age, and the method used to extract the APF is different from the one used in this study. This could explain these mixed findings.

Here we reported that a high CR was associated with a slowing of APF in older people with SMCs. This relationship could reveal a compensatory effect of CR on the mechanisms that modulate alpha rhythms. In AD patients, the compensatory effect of CR has been associated with increased indicators of brain pathology, such as reduced brain metabolism, increased amyloid deposition, or increased rates of atrophy (Vaqué-Alcázar et al., 2017). This suggests that compensatory reserve mechanisms reflect a greater ability to tolerate brain damage.

In young people, the picture was quite different. In fact, those who showed some correlations were participants in the control groups. Specifically, young people in the control group with high CR elicited higher alpha amplitudes than young people with SMCs. This relationship has not been previously reported in young samples. There is currently great interest in relating neural functioning to CR in people with AD (Babiloni et al., 2020b). The association between two correlated variables with regard to changes in one of two variables that are not necessarily parallel across conditions and age groups, as demonstrated here with CR and alpha amplitude, adds important information to help to understand the directionality and causality of the relationship between indicators of neural functioning and CR. In this context, future studies should analyze whether, based on CR, alpha parameters can be useful first-level biomarkers in prevention programs developed for older adults with SMCs.

Taken together, the present findings are also an important complement to the literature reporting high stability of APF and the alpha amplitude parameter in the absence of pathology, as shown by healthy people with SMCs. This suggests that substantial changes in these parameters might be indicative of a pathological process (Babiloni et al., 2009). Although the link between APF and CR found in this study paves the way for future studies on the neural mechanisms underpinning this relationship, a larger sample size and current analyses of

functional brain changes would be needed to confirm our findings. Additionally, longitudinal follow-up studies could provide insight into the evolution of these peak parameters.

CHAPTER 7.
GENERAL DISCUSSION

The previous chapters have described the main findings related to the behavioral evidence and neural correlates of facial emotion processing in both young and older people with SMCs in comparison with people without SMCs. In addition, the relationship between facial emotion processing and EF has been shown in older people with SMCs. Power spectral change in frequency bands in young and older people with and without SMCs has also been investigated. In addition, we have studied the EEG reactivity in all frequency bands and its correlation with neuropsychological measures, as well as alpha peak parameters (APF and alpha amplitude) and their relationship with CR. This final chapter presents a summary of the main results of these studies.

7.1 MAIN FINDINGS

7.1.1 Facial emotion processing in young people with subjective memory complaints

Evidence that facial emotion processing is sensitive to the attentional resources (Luo et al., 2010), which are altered in young people with SMCs (Ruiz-Sanchez de Leon et al., 2010), has provoked interest. Therefore, the first aim of this thesis, addressed in Chapter 3, was to determine whether facial emotion processing is different in young people with and without SMCs, exploring behavioral data (RT and accuracy) as well as latencies and amplitudes of the N170 and LPP components. To do so, participants were exposed to positive, negative, and neutral human facial expression images extracted from the KDEF, and they completed the MFE-30 scale. Regarding behavioral data, neither RT nor accuracy was significantly different between the SMCs and noSMCs groups. Regardless of the group and sex, participants showed more accuracy for positive valences. Concerning ERPs, we found that participants with SMCs

elicited lower amplitudes in the N170 component, compared to noSMCs. Smaller N170 amplitude elicited by people with SMCs might reflect emotional processing difficulties because N170 is considered a neural indicator of facial structure encoding (Bentin et al., 1996) and emotional valence processing (Qiu et al., 2017). Specifically, the N170 amplitude was lower for positive and neutral faces in SMCs compared to noSMCs; that is, young people with SMCs showed a deficit in attentional resources only for early processing of positive and neutral emotions, whereas negative faces elicited the same amplitude in young adults with and without SMCs. This finding might be interpreted from a biological viewpoint, given that negative face detection is relevant for survival because this expression is a sign of potential harm (Calvo & Beltrán, 2013). Contrary to what was hypothesized, there were no differences in the latencies of the N170 and LPP components. In addition, women with SMCs showed longer latencies in N170 for neutral faces compared to women noSMCs. Moreover, we observed that women showed higher amplitudes than men on both the N170 and LPP components. Although sex differences have shown contradictory results (Herlitz & Lovén, 2013; Verhallen et al., 2017), our finding is in line with Proverbio (2017). This author reported that women have advantages over men in the processing of emotional faces, which would suggest greater interest in social information and a more empathetic attitude in women than in men.

Finally, for the LPP component, no differences depending on SMCs were found in latency and amplitude. This lack of effect indicates that young people with SMCs would not present difficulties in the late processing related to a greater evaluation of the affective valence of a face (Luo et al., 2010).

7.1.2 Facial emotion processing and its relationship with executive function in older people with subjective memory complaints

Deficits in facial emotion processing and EF have been extensively investigated in MCI and AD (Bora & Yener, 2017; Cespón et al., 2018; Elferink et al., 2015; Stenfors et al., 2013). Because SMCs are considered a risk factor for developing these disorders (Cantero et al., 2016), the second aim of this thesis, addressed in Chapter 4, was to analyze whether these deficits also occur in older people with SMCs, as proposed in some studies (Asaumi et al., 2014; Pietschnig et al., 2015; Sarabia-Cobo et al., 2015). To do so, we compared behavioral and ERPs data between older people with and without SMCs during the KDEF task. Participants also answered a neuropsychological battery to assess EF (i.e., verbal working memory, visuo-spatial working memory, attention-switching, and verbal fluency) and completed the MFE-30 scale.

Results showed that older people with SMCs were slower and less accurate than controls, as was also observed in MCI and AD (Pietschnig et al., 2015; Teng et al., 2007; Varjassyová et al., 2012;Yang et al., 2015). At the ERPs level, men with SMCs revealed longer latencies in the N170 component for positive, negative, and neutral faces than women with SMCs. This finding adds neural evidence to a prior study conducted with behavioral data in SMCs (Pietschnig et al., 2015). However, we failed to find differences in P300 or LPP latencies or amplitudes in older people with and without SMCs, which indicates that later processing phases of emotional faces may be preserved in older people with SMCs. In addition, higher P300 and LPP amplitudes for negative vs. neutral faces were associated with better performance on verbal and visuospatial working memory, psychomotor speed, and attention. Increased amplitudes in these components would reflect a greater cognitive effort (Phillips et al., 2008). Regarding sex differences, we found better performance by women than men, regardless of the group, across both behavioral and ERPs data. Therefore, our results indicate

that older people with SMCs show deficits in facial emotion processing that affect early phases of face structure encoding and emotional valence processing. Moreover, the associations between the P300 and LPP components and EF test performance suggest that deficits in EF could cause problems in processing emotional faces. These deficits could be due to the progressive degeneration of the brain structures modulating this process (Pietschnig et al., 2015; Teng et al., 2007).

7.1.3 EEG markers and subjective memory complaints

Resting state EEG rhythms are an important tool to evaluate oscillatory signals such as spectral power at frequency band (Lejko et al., 2020) and EEG reactivity (Fröhlich et al., 2021). Studies in patients with MCI and AD have reported important power spectral changes, such as increments in delta and theta power and decreases in beta power in early phases of AD, followed by a decrease in alpha power in later stages of AD (Babiloni et al., 2006; 2012; Hatz et al., 2013; Michels et al., 2017; Roh et al., 2011). The third aim of this thesis was to investigate the spectral power of frequency bands and EEG reactivity in older and young people with and without SMCs, and determine whether there is a correlation between the region and specific spectral powers and EEG reactivity and neuropsychological measures. To do so, young and older people underwent three minutes of EEG recording in a resting-state with their EC and EO. Then they completed several neuropsychological tests.

Results presented in Chapter 5 showed that, compared to controls, older people with SMCs had increased theta power and a subtle loss of alpha reactivity in EO. A previous study in older people with SMCs also observed this increase in the theta band (Alexander et al., 2006). In addition, in older people with SMCs in the EO condition, we found that increased spectral power of the theta, beta and delta bands was associated with better verbal memory,

whereas higher delta spectral power was associated with better attention performance. Studies carried out in older people have shown similar associations between theta and verbal memory (Alexander et al., 2006). In the EC condition, higher beta spectral power was associated with better verbal memory and EF performance. Likewise, higher beta and delta EEG reactivity were associated with better EF and attention performance, respectively.

Despite these findings in older people with SMCs, we failed to find significant differences across spectral power and EEG reactivity in young people with SMCs. This null result could indicate that brain activity is preserved in this population. However, in the correlation analysis, we observed an opposite effect in young people compared to older ones. Specifically, lower spectral power in theta and beta bands was related to worse performance in verbal memory and EF. Additionally, reduced beta EEG reactivity was related to worse verbal memory, EF, and attention performance. These findings suggest that EEG changes may be nonlinear across age in people with SMCs. In summary, results addressing the third aim of this thesis showed that some neurophysiological markers of brain dysfunction may identify cognitive decline and changes before they are observed on objective neuropsychological tests.

7.1.4 Alpha peak parameters and cognitive reserve in people with subjective memory complaints

Although some studies have investigated the association between SMCs and objective memory performance, the results are inconsistent (Zlatar et al., 2018). This lack of association has led to examining whether people with greater CR might have more accessible resources with which to confront cognitive decline over time (Lojo-Seoane et al., 2018). In addition, alpha peak parameters, such as APF and amplitude, were slower and reduced, respectively, in MCI patients (Garcés et al., 2013). The fourth objective of this thesis was to investigate whether alpha peak parameters, such as APF and amplitude, were different in people with and without

SMCs, and explore age and sex-related changes. In addition, the relationship between CR and APF in people with SMCs and controls was studied. To do so, resting state eyes-closed EEG data were recorded for three minutes. In addition, participants completed the Cognitive Reserve Questionnaire.

Results presented in Chapter 5 showed no differences in APF or alpha amplitude between older and young people with SMCs and controls. Moreover, no significant sex differences were detected. Regardless of the condition and sex, we replicate previous findings showing decreased amplitude in older people compared to younger people. In addition, in older people with SMCs, high CR was significantly correlated with slowing APF. By contrast, in young people in the control group, high CR was correlated with a greater Pz, P3, and O2 amplitude. Although previous studies have reported a slowing of APF and decreased amplitude in MCI (Garcés et al., 2013) and a reduced mean APF in AD (Ruiz-Gómez et al., 2018), the hypothesis that alpha peak parameters in SMCs would be slower compared to a control population was not confirmed in our sample. Furthermore, the alpha peak parameters are not determined solely by the pathology, but they also depend on other factors such as age or sex. Older and young adults had similar APF; in contrast, amplitudes were significantly reduced in older people, especially in the occipital regions, leading to the conclusion that, although no slowing of APF was seen, alpha production might be compromised in older people. The pattern of results observed in this study provides an important complement to the literature reporting high stability of APF and alpha amplitude parameters over time in the absence of pathology, as shown by healthy people with SMCs. This suggests that substantial changes in these parameters might be indicative of a pathological process, such as disease progression (Babiloni et al., 2009). In addition, the relationship between APF and CR found in this study in older people with SMCs could reveal a compensatory effect of CR on the mechanisms that modulate

alpha rhythms. Therefore, these alpha parameters could easily be candidates for monitoring deviations from normal brain function, such as disease progression.

7.2 LIMITATIONS, STRENGTHS, AND FUTURE RESEARCH

In each chapter, specific limitations have been considered. Here, some general limitations of the thesis are presented. In Chapters 3 and 4, pictures of human emotion facial expression were used as stimuli for studying facial emotion processing in SMCs. Although a set of standardized affective stimuli were utilized (Lundqvist et al., 1998), the stimuli were static and grayscale pictures of faces, which lack a real effect that people can use to recognize facial expressions in natural contexts and elicit physiological responses. All the participants in this study were volunteers who attended the university. This meant that the sample was composed of healthy, well-educated participants. Education level is also an important factor because it is known to be a proxy for CR, and it can modulate the relationship between neural correlates and performance measured on a neuropsychological test (Liu et al., 2013). Therefore, this above-average level of education may not be representative of the population and could make the results difficult to generalize. Another limitation is that, although the majority of the electrophysiological studies use similar sample size, a larger sample size would be necessary to increase the statistical power. This is specifically important in Chapters 3 and 4, where sex is considered a within-subject factor. Finally, our design is a cross-sectional approach, which limits the extent to which we can identify brain and cognition changes in people with SMCs. Thus, the differences between SMCs and controls may only emerge in a longitudinal study.

Despite these limitations, it is important to highlight some strengths, such as the rigorous inclusion criteria and the effort made to record, store, and carefully analyze the ERPs components and resting state EEG rhythms. The aforementioned limitations motivate us to develop future studies using colors and high quality 3-dimensional photographs of facial

expressions to provide a more real effect for emotion recognition (Gur et al., 2002). Additionally, demographic, psychological, and non-affective factors that interact with the affective modulation of the ERPs could be added. These findings should also be replicated in follow-up studies to explore whether brain or cognitive changes are related to SMCs, and whether they are indeed a risk factor for developing dementia-related disorders. Furthermore, future studies should use larger samples in order to increase the statistical power to detect a triple interaction (i.e., Emotional Valence x Sex x Group).

CHAPTER 8.
MAIN CONCLUSIONS

In this section, the most important conclusions stemming from the objectives of this thesis are the following:

1. Young adults with SMCs have difficulties in the early stage of emotional processing, as evidenced by differences from young people without SMCs in N170 amplitudes.

2. Behavioral performance and the last stages of emotional processing, as shown by the LPP component, were similar in young people with and without SMCs. This suggests that sustained attention to emotional faces is conserved in young people with SMCs.

3. There are sex differences in young people, regardless of the group, with women showing better processing of emotional faces than men. This was evidenced by high amplitudes in the first and last emotional processing stages.

4. Older people with SMCs showed deficits in the early phases of face structure encoding and emotional valence processing that were evidenced by longer RT and less accuracy.

5. Likewise, older men with SMCs revealed more difficulties in the first stage of emotional processing, as shown by the longer latencies elicited on all the emotional valences.

6. Older people with SMCs showed similar latencies and amplitudes in the later components (P300 and LPP) as those without SMCs, suggesting that later and more complex stages of emotional processing remain preserved in this population.

7. Later components (P300 and LPP) are positively associated with EF, suggesting that EF deficits are likely to cause problems in facial emotion processing.

8. Older people with SMCs are characterized by distinct power resting state EEG rhythms, specifically at increased theta power, and a subtle loss of EEG reactivity in EO, which suggests that neurophysiological markers of brain dysfunction may identify cognitive decline and changes before they are observed on objective neuropsychological tests.

9. Young people with SMCs, compared to controls, have relatively preserved electrical brain activity, as demonstrated by the lack of difference in the spectral power of the bands and EEG reactivity.

10. The association of spectral power and EEG reactivity with neuropsychological assessments points to a nonlinear progression in neurophysiological changes from young people with SMCs to older people with SMCs.

11. APF and alpha amplitude show no significant differences between people with and without SMCs; therefore, these alpha parameters could be easy candidates to monitor deviations from normal brain function.

12. Older and young adults had similar APF; however, amplitudes were significantly reduced in older people compared to younger people, especially in the occipital regions.

13. There are no sex differences in APF or alpha amplitudes in people with and without SMCs.

14. The association between high CR and slowing of APF in older people with SMCs could reveal a compensatory effect of CR on the mechanisms that modulate alpha rhythms.

CHAPTER 9.
GENERAL SUMMARY IN SPANISH

Con el envejecimiento de la población, ha aumentado el interés por las preocupaciones acerca de los cambios cognitivos, pues cada vez son más las personas que acuden al médico con tales preocupaciones buscando ayuda (Brailean et al., 2019). Estos cambios en la capacidad cognitiva se reflejan en la percepción subjetiva de las personas afectadas. A esta percepción se le denominó quejas subjetivas de memoria (SMCs, ver abreviatura en inglés; Subjective Memory Complaints). Este concepto ha sido definido como la conciencia subjetiva de la pérdida de memoria en ausencia de cualquier condición orgánica o identificable en las evaluaciones neuropsicológicas (Schmand et al., 1996). Aunque las SMCs son reportadas frecuentemente por personas mayores (Jacob et al., 2019; Meyer et al., 2017; Montejo et al., 2019; Vlachos et al., 2019), muchos jóvenes también han manifestado tener dificultades con su memoria (Ginó et al., 2010; Rowell et al., 2015; Sohrabi et al., 2018; Loprinzi, 2019; Mendes et al., 2008). Además, las SMCs han sido consideradas un factor de riesgo para desarrollar trastornos relacionados con demencias como el deterioro cognitivo leve (MCI, ver abreviatura en inglés; Mild Cognitive Impairment) y enfermedad de Alzheimer (AD, ver abreviatura en inglés; Alzheimer Disease; ver revisión: Abdulrab & Heun, 2008).

Un aspecto importante para comprender las SMCs es determinar en qué medida se relacionan con el desempeño objetivo en las pruebas cognitivas. Diferentes estudios llevados a cabo tanto en mayores como en jóvenes han arrojado resultados inconsistentes. Algunos han encontrado que las SMCs se relacionan con peor desempeño mnésico (Burmester et al., 2016; Brailean et al., 2019; Cespón et al., 2018; Kim et al., 2017; Vaskivuo et al., 2018), mientras que otros no encuentran tal relación (Lazarou et al., 2018; Lee et al., 2017; Park et al., 2019; Rowell et al., 2015; Zlatar et al., 2018). Estas inconsistencias han planteado la necesidad de estudiar otras variables que permitan llegar a entender las SMCs, tales como las variables neurofisiológicas. En este sentido, el procesamiento de emociones faciales, que es una importante función cognitiva comúnmente afectada en personas diagnosticadas de trastornos

relacionados con demencias, podría ayudar a analizar cambios cerebrales funcionales que se pueden producir en las personas con SMCs.

Las expresiones faciales son un componente clave del funcionamiento y las relaciones sociales y reconocerlas adecuadamente es un prerrequisito para una óptima calidad de vida. Los déficits en el reconocimiento de expresiones faciales han sido ampliamente estudiados en MCI (Bora & Yener, 2017) y AD (Elferink et al., 2015). Evidencias previas también encontraron sutiles dificultades en el procesamiento emocional en personas mayores con SMCs (Lazarou et al., 2018; Pietschnig et al., 2015). El procesamiento de caras emocionales incluye un complejo sistema de estructuras cerebrales como la amígdala, la ínsula, las regiones ventrales de la circunvolución cingulada anterior y la corteza prefrontal (Phillips et al., 2003), la corteza temporal occipital inferior, la circunvolución fusiforme (Eimer & Holmes, 2007), los ganglios basales y las cortezas parietales derechas (Adolphs, 2002). Algunos estudios han demostrado que estas estructuras también se encuentran alteradas en las SMCs (Hafkemeijer et al., 2013; Van Flier et al., 2004). Por ello, es importante profundizar en el estudio del procesamiento emocional mediante técnicas no invasivas para detectar lo antes posible déficits en el proceso neurodegenerativo asociado a trastornos relacionados con las demencias.

El procesamiento emocional de expresiones faciales puede ser investigado usando una técnica relativamente económica, no invasiva y con alta resolución temporal como el electroencefalograma (EEG, ver abreviatura en inglés; Electroencephalogram). Esta técnica abre la puerta a nuevas posibilidades para explorar la emoción y cognición humana en el momento en que ocurren. En este sentido los potenciales relacionados con eventos (ERPs, ver su abreviatura en inglés; Event-related Potentials) permiten medir la actividad neuronal y, en concreto, el procesamiento de la información emocional con una resolución temporal de milisegundos (Olofsson et al., 2008). Los estímulos emocionales modulan un amplio rango de ERPs, comenzando con el procesamiento perceptivo temprano reflejado en el componente

N170, hasta componentes que representan fases de procesamiento de estímulos emocionales de orden superior como el P300 y el LPP (Luo et al., 2010; Schupp et al., 2006).

Otra forma de explorar cambios en la funcionalidad del cerebro en las personas con SMCs es registrando los ritmos electroencefalográficos en estado de reposo. Esto no requiere estimulación y no se ve afectado por la fatiga, el meta-aprendizaje y la ansiedad, generalmente asociados con el desempeño de la tarea (Babiloni et al., 2016). Estos ritmos se registran en el cuero cabelludo de las personas durante períodos breves (es decir, minutos) con los ojos cerrados (EC, ver su abreviatura en inglés; Eyes Closed) y los ojos abiertos (EO, ver su abreviatura en inglés; Eyes Open) (Babiloni et al., 2020a). Las medidas más utilizadas son el análisis de la potencia espectral, la reactividad del EEG y la frecuencia del pico de alpha (APF) (Alexander et al., 2006; Lejko et al., 2020; Ruiz-Gómez et al., 2018). Específicamente, cuando se comparan con controles sanos, los sujetos con MCI y AD presentan un incremento de delta y theta y una disminución en la potencia de las bandas alpha y beta en comparación con los sanos (Babiloni et al., 2012; Hatz et al., 2013; Michels et al., 2017; Wan et al., 2018), así como una reactividad disminuida en la banda alpha (Fröhlich et al., 2021). Respecto a la APF, un estudio previo observó que los pacientes con MCI presentaban una APF más baja en comparación con los controles, y significativamente más alta en comparación con los pacientes con AD (Fernández et al., 2006). Finalmente, un constructo al que se ha aludido para explicar las SMCs es la reserva cognitiva (CR; ver su abreviatura en inglés; Cognitive Reserve). La CR se ha utilizado para explicar por qué dos personas pueden tener diferentes manifestaciones clínicas de la misma enfermedad (Stern, 2012) y se ha planteado que las personas con mayor CR podrían tener más recursos accesibles para afrontar el deterioro cognitivo a lo largo del tiempo (Lojo-Seoane et al., 2018). Por tanto, es importante identificar estos marcadores neurofisiológicos tempranos fiables para la detección y planificación de futuros tratamientos de personas con riesgo de sufrir MCI y AD.

En resumen, el objetivo general de esta tesis ha sido avanzar en el conocimiento de algunos factores neurofisiológicos que pudieran permitir identificar el deterioro y los cambios cognitivos antes de que sean observados en las pruebas neuropsicológicas. Para ello, hemos estudiado el procesamiento emocional facial y algunos correlatos neurofisiológicos, el rendimiento objetivo en pruebas neuropsicológicas, la potencia espectral, la reactividad a la apertura de ojos en estado de reposo, la APF y amplitud de Alpha y la CR.

9.1 OBJETIVOS E HIPÓTESIS

Debido a la inconsistencia de los resultados y las cuestiones pendientes expuestas en el capítulo 1 (Introducción), la presente tesis pretende abordar los siguientes objetivos generales y específicos en base a las hipótesis planteadas:

Objetivo general 1. Examinar si el procesamiento de las emociones faciales es diferente en jóvenes con y sin SMCs expuestos a caras positivas, negativas y neutras mediante medidas conductuales y el registro de los ERPs.

Objetivo específico 1.1: Investigar las diferencias en las medidas de comportamiento, es decir, tiempo de reacción (RT, ver abreviatura en inglés; Reaction Time) y precisión en jóvenes con y sin SMCs.

Objetivo específico 1.2: Estudiar las diferencias en latencias y amplitudes de los componentes N170 y LPP en jóvenes con y sin SMCs.

Objetivo específico 1.3: Explorar las posibles diferencias relacionadas con el sexo en el procesamiento de la emoción facial entre jóvenes con y sin SMCs.

Dado que el procesamiento de las emociones faciales no se ha abordado en jóvenes con SMCs, basamos nuestras hipótesis en un modelo hipotético sobre las funciones cognitivas involucradas en el procesamiento de las caras emocionales (Luo et al., 2010). Este modelo

propone que el procesamiento de la expresión emocional de las caras puede ser modulado por recursos atencionales. Así, cuando los recursos atencionales son abundantes, se observan mayores amplitudes y menores latencias. Dado que investigaciones previas han encontrado dificultades atencionales en jóvenes con SMCs (Ruiz-Sánchez de León et al., 2010), esperábamos latencias más largas y amplitudes más pequeñas en los componentes N170 y LPP en participantes con SMCs, en comparación a aquellos sin SMCs. También planteamos la hipótesis de RT más cortos, mejor precisión, latencias más cortas y mayores amplitudes de N170 y LPP en mujeres que en hombres (Choi et al., 2015; Hampson et al., 2006; Sun et al., 2017).

Estos objetivos, así como los principales resultados obtenidos han sido presentados en el capítulo 3.

Objetivo general 2. Investigar si existen diferencias en los correlatos neuronales y medidas conductuales del procesamiento de emociones faciales y su relación con la función ejecutiva (EF, ver su abreviatura en inglés; Executive Function) entre personas mayores con y sin SMCs.

Objetivo específico 2.1: Estudiar las diferencias en las medidas de comportamiento (es decir, RT y precisión) en personas mayores con y sin SMCs.

Objetivo específico 2.2: Analizar las diferencias en latencias y amplitudes de los componentes N170, P300 y LPP en personas mayores con y sin SMCs.

Objetivo específico 2.3: Explorar la posible asociación entre las amplitudes de N170, P300 y LPP y el rendimiento de las EF, evaluadas con diversas pruebas neuropsicológicas, en personas mayores con y sin SMCs.

Objetivo específico 2.4: Investigar las posibles diferencias relacionadas con el sexo en el procesamiento de la emoción facial en personas mayores con y sin SMCs.

Basándonos en estudios anteriores realizados en personas con MCI, planteamos la hipótesis de que las personas mayores con SMCs mostrarían un RT más lento y peor precisión en comparación con el grupo control (Sarabia-Cobo et al., 2015; Schefter et al., 2013; Yang et al., 2015). Además, también anticipamos diferencias en los ERPs. Específicamente, esperamos latencias más largas y amplitudes más pequeñas en N170, P300 y LPP en los participantes con SMCs en comparación con los controles (Asaumi et al., 2014; Schefter et al., 2013; Yang et al., 2015). Debido a que la asociación entre EF y ERPs no se ha estudiado previamente en personas mayores con SMCs, no teníamos una hipótesis para esta asociación. Finalmente, dado que los estudios psicológicos (Montagne et al., 2005) y fisiológicos (Choi et al., 2015; Li et al., 2008) han mostrado diferencias sexuales en el procesamiento de emociones faciales, exploramos posibles diferencias relacionadas con el sexo en las personas con SMCs y grupos control.

Estos objetivos se han abordado en el capítulo 4 de esta tesis.

Objetivo general 3. Investigar si los ritmos del EEG en estado de reposo, normalmente alterados en el MCI y AD y la reactividad del EEG, se ven afectados en las personas mayores y jóvenes con SMCs en comparación con las personas control.

Objetivo específico 3.1: Determinar la potencia espectral de las bandas de frecuencia en personas mayores y jóvenes con y sin SMCs.

Objetivo específico 3.2: Analizar la reactividad del EEG a la EO en personas mayores y jóvenes con y sin SMCs.

Objetivo específico 3.3: Explorar si existe una correlación entre las regiones y potencias espectrales y EEG reactividad específicas y medidas neuropsicológicas en personas mayores y jóvenes con y sin SMCs.

Para este estudio formulamos hipótesis de trabajo basadas en estudios previos de personas con MCI y AD. Propusimos que los ritmos corticales del EEG, generalmente alterados en estas patologías (es decir, disminución de ondas rápidas y aumento en ondas lentas), también se verían afectados en las personas con SMCs en comparación con las del grupo control, como un posible marcador temprano de procesos patológicos subyacentes (Alexander et al., 2006; Babiloni et al., 2010). La segunda hipótesis fue que la reactividad del EEG sería similar en todas las bandas de frecuencia en ambos grupos (SMCs y control), basándonos en hallazgos anteriores (Alexander et al., 2011; Fröhlich et al., 2021). Por último, planteamos la hipótesis de que en las personas con SMCs, la alteración del EEG en estado de reposo correlacionaría con una peor función cognitiva (Babiloni et al., 2013; Gaubert et al., 2019).

En el capítulo 5 planteamos los resultados obtenidos para responder a estos objetivos.

Objetivo general 4. Investigar los parámetros de pico alpha, como APF y amplitud, para las personas con SMCs y del grupo control. Además, exploramos si estos parámetros no solo difieren entre SMCs y controles, sino también entre jóvenes y mayores, así como por sexos.

Objetivo específico 4.1: Examinar el APF y la amplitud en personas con SMCs y del grupo control.

Objetivo específico 4.2: Investigar las posibles diferencias en personas jóvenes y mayores, así como las diferencias relacionadas con el sexo en el APF y la amplitud.

Objetivo específico 4.3: Explorar si existe una relación entre CR y APF y la amplitud alpha en el contexto de las SMCs en cada grupo de edad (mayores y jóvenes).

Con base en la literatura previa en MCI y AD, planteamos que las personas mayores con SMCs también mostrarían un APF más bajo y una amplitud reducida en comparación con el grupo control (Garcés et al., 2013; Ruiz-Gómez et al., 2018). Además, en el contexto de las diferencias fisiológicas relacionadas con la edad, los parámetros del pico de alpha podrían relentizarse, como se ha encontrado en un estudio anterior (Scally et al., 2018). Debido a que aún no se han determinado las diferencias relacionadas con el sexo en las personas con SMCs, no teníamos hipótesis específicas al respecto. Finalmente, aunque hasta el momento no se han realizado estudios de la relación entre CR y APF y amplitud, examinamos esta correlación considerando que la CR ha mostrado efectos protectores frente al deterioro cognitivo (Lojo-Seoane et al., 2018).

En el capítulo 6 hemos planteado responder a estos objetivos de investigación.

9.2 METODOLOGÍA

Con el fin de proporcionar una visión integral de la metodología utilizada en la presente tesis, en esta sección se realiza un breve resumen sobre las características de los participantes, el procedimiento y las variables evaluadas.

9.2.1 Participantes

La muestra de la presente tesis proviene, por un lado, de diferentes facultades de la Universitat de València, siendo, por tanto, estudiantes de diferentes grados, y, por otro lado, de un programa de estudios de la Universitat de València para personas mayores de 55 años (NAU GRAN). Se reclutaron en total 83 participantes mayores (41 hombres y 42 mujeres; 40 SMCs

y 43 controles) y 82 participantes jóvenes (42 hombres y 40 mujeres; 44 SMCs y 38 controles). El número de la muestra varió dependiendo de los objetivos de los estudios que forman parte de esta tesis. Los criterios de exclusión fueron: antecedentes de abuso de alcohol o drogas; fumar más de 10 cigarrillos al día; haber sido operado bajo anestesia general en el último año; presencia de problemas severos de visión o audición o alguna enfermedad que implique una alteración del sistema nervioso; y padecer un trastorno neurológico o psiquiátrico. Además, los participantes fueron excluidos si tomaban medicamentos que pudieran afectar la función cognitiva o emocional, sustancias psicotrópicas, betabloqueantes o benzodiazepinas, o si habían experimentado un evento estresante en los últimos seis meses. Todos los participantes eran diestros.

9.2.2 Procedimiento

Las sesiones experimentales tuvieron una duración de 2 h y se realizaron, por la mañana (entre las 10:00 y las 14:00 h) o por la tarde (entre las 15:00 y las 19:00 h). Cada participante asistió a dos sesiones individuales en dos días consecutivos, la mitad lo hizo en el turno de la mañana y la otra mitad en el turno de la tarde. Se indicó a los participantes que, el día de antes de la sesión, debían abstenerse de realizar actividad física intensa, no debían consumir alcohol ni ningún otro estimulante desde la noche anterior, y debían dormir tanto como de costumbre. También se les indicó que, al menos 1 hora antes de la sesión, debían beber solo agua, y no comer, fumar, tomar estimulantes (como café, cola, cafeína, té o chocolate).

Una vez en el laboratorio, en la primera sesión, los participantes completaron los cuestionarios de Fallos de Memoria Cotidiana (MFE-30), el Inventario de Depresión de Beck-II (BDI-II), un Cuestionario General con datos demográficos y el Cuestionario de Reserva Cognitiva. Luego, se realizó una evaluación neuropsicológica con el fin de valorar su atención

y memoria de trabajo (Digit Span Test; DS-forward and DS- Backward), memoria de trabajo visuoespacial (AWMA; Dot Matrix Backward and Dot Matrix-Forward), cambios de atención; (Trail-Making Test A y B; TMT), fluidez verbal (Fonológica y Semántica), memoria verbal (FCSRT), y el control de interferencia (Test de Stroop).

Durante la segunda sesión, a los participantes se les presentó una tarea de procesamiento emocional que contenía 204 imágenes con caras que expresaban emociones positivas, negativas y neutras. Durante la realización de dicha tarea, se registró la señal del EEG usando un sistema de 29 canales y se evaluaron los ERPs.

Por otro lado, se registró el EEG durante tres minutos en estado de reposo en dos condiciones, EC y EO, con el objetivo de obtener medidas de potencia espectral para las bandas delta, theta, alpha, beta, la reactividad a los EO y la APF y amplitud de alpha.

9.2.3 Variables neurofisiológicas

Para estudiar el procesamiento emocional, la señal de EEG se recolectó de acuerdo con el sistema internacional 10–20 (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, FCz, M1, T3, C3, Cz, C4, M2, P3, P4, Pz, P4, T5, T6, O1, Oz y O2). El electrodo AFz se usó como sistema de tierra y los electrodos se referenciaron a FCz durante el registro. El componente N170 se midió en T6 y T5 dentro de la ventana de tiempo de 130 a 200 ms. Los componentes P300 y LPP se midieron en Pz dentro de las ventanas temporales de 200–500 ms y 400–700, respectivamente. Para investigar el rendimiento del comportamiento en la tarea de procesamiento emocional facial, también se calcularon los RT promedio y la precisión.

Para estudiar el estado de reposo, las bandas de frecuencia de interés fueron: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8-12 Hz), y beta (13–30 Hz). Se estimó la densidad espectral de potencia promedio para cada condición de reposo (EC/EO). El análisis espectral de potencia se

realizó aplicando una transformada rápida de Fourier (FFT, ver abreviatura en inglés; Fast Fourier Transform). Los electrodos se agruparon en cinco regiones corticales de interés: frontal (F3, Fz, F4), central (C3, Cz, C4), parietal (P3, Pz, P4), occipital (O1, O2), temporal (T3, T4, T5, T6). Las potencias espectrales se transformaron logarítmicamente antes del análisis estadístico. Para estudiar la reactividad a EO, se restó el logaritmo de la potencia de ojos abiertos, al logaritmo de la potencia de ojos cerrados, en cada banda de frecuencia. La APF se estimó como la frecuencia del pico alpha a partir del espectro medio sobre 6 electrodos posteriores (Pz, P4, P3, Oz, O2, O1) mediante la detección de picos entre 8 y 12 Hz. Se calculó APF y la amplitud para cada participante involucrado en el estudio. La amplitud alpha se definió como la amplitud media de los seis electrodos posteriores.

9.2.4 Tarea de estímulo facial

Los estímulos fueron 204 expresiones faciales de emociones con valencias positivas, negativas y neutras. Se utilizaron 68 fotos para cada valencia, con modelos masculinos y femeninos en igual proporción presentados aleatoriamente. Todas las fotos se extrajeron de la base de datos Karolinska Emotional Directed Faces (Lundqvist et al., 1998).

Los estímulos se presentaron en la siguiente secuencia: (1) apareció una marca de fijación (+) durante 1000 a 1300 ms; (2) la cara se presentó durante 200 ms; y (3) se mostró una pantalla en blanco durante 800 ms. Las imágenes se presentaron utilizando el software E-prime (v2.0).

9.2.5 Evaluación neuropsicológica

La *memoria de trabajo verbal* se evaluó con la prueba Digit Span del Wechsler Memory Scale (Wechsler, 1997). Esta prueba consta de dos subpruebas (a) Digit Span Forward, una medida de atención; y (b) Digit Span Backward, una medida del componente ejecutivo de la memoria de trabajo (Conklin et al., 2000). En la prueba hacia adelante el participante escucha números y tiene que repetirlos en el mismo orden. En la prueba hacia atrás el participante escucha números y tiene que repetirlos en orden inverso. En esta tarea, las secuencias comienzan en el nivel 2 y pueden aumentar hasta el nivel 8. Se obtuvieron dos medidas: (a) número total de ensayos recordados correctamente en el mismo orden; y (b) número total de intentos recordados correctamente en el orden inverso.

La memoria de trabajo visuoespacial se evaluó con la prueba AWMA (Alloway et al., 2008). En la subprueba Dot Matrix Forward, los participantes señalan los puntos rojos en el mismo orden en que aparecieron. En la subprueba Dot Matrix Backward, los participantes señalan los cuadros en el orden inverso al que aparecen. Se obtuvieron dos medidas: (a) número total de intentos correctos en el mismo orden; y (b) número total de intentos correctos en el orden inverso. En esta tarea, las secuencias comienzan en el nivel 2 y pueden aumentar hasta el nivel 8.

Los *cambios de atención* se valoraron con el TMT. Esta prueba consta de dos formas: TMT-A y la TMT-B. El TMT-A se usó para evaluar la atención y la velocidad psicomotora general, y el TMT-B se administró para medir la eficiencia del rendimiento del cambio de atención (Reitan, 1992), un componente de la EF. En el TMT-A, los participantes deben conectar en orden creciente unos círculos numerados del 1 al 25. En el TMT-B, los participantes deben conectar círculos numerados del 1 al 13 y letras de la A a la L, alternando

números y letras. La puntuación obtenida es la cantidad de segundos necesarios para finalizar cada prueba.

Para evaluar la *fluidez verbal* se les pidió a los participantes que generaran tantas palabras como fuera posible comenzando con las letras F, A y S en 60 s. Además, para evaluar la *fluidez semántica*, se pidió también que generaran tantas palabras como fuera posible en la categoría semántica "Animales" en 60 s. Sólo se puntuaron las respuestas correctas; no se consideraron intrusiones, intentos repetidos y variaciones dentro de la misma especie. Las instrucciones se dieron siguiendo los procedimientos proporcionados en la prueba de Barcelona (Peña-Casanova, 1991). La puntuación obtenida fue el número de palabras correctas enumeradas en cada categoría.

La *memoria verbal* se evaluó mediante la prueba FCSRT en su versión en español (Peña-Casanova, 1991). Esta consiste en una lista de 16 palabras donde el participante tiene que identificar cada palabra con respecto a una pregunta, por ejemplo ¿cuál es un pájaro?. Luego comienza la tarea de distracción, donde el participante tiene que restar números de 3 en 3 durante 20 segundos. Después de eso, comienza la recuperación libre durante 90 segundos. En la recuperación facilitada el experimentador hace al participante preguntas facilitadoras sobre la palabra que no ha recordado en la recuperación libre. El mismo proceso se repite en tres ensayos. De esta tarea se obtuvieron cinco índices: (a) recuerdo libre del primer ensayo, puntuación máxima: 16; (b) recuerdo libre total: suma de recuerdo libre de los 3 intentos, puntuación máxima: 48; (c) recuerdo total: suma del recuerdo libre total y el recuerdo facilitado total, puntuación máxima: 48; (d) recuerdo libre diferido: suma del total de recuerdo diferido libre, puntuación máxima: 16; (e) recuerdo diferido total: suma del total de recuperación diferida libre y diferida facilitada.

El *control de interferencia* se evaluó con la prueba Stroop Colour-Word Interference (Golden, 1978). Esta tarea contiene tres partes: página de palabras (los nombres de los colores impresos en tinta negra), página en color (líneas de X impresas en tinta de color) y página de palabras en color (los significados de las palabras y los colores de tinta no coinciden). En cada tarea, los participantes tuvieron que leer palabras o nombrar los colores de la tinta lo más rápido posible durante 45 segundos. En la primera prueba, los participantes deben leer la palabra escrita (P) (rojo, azul o verde). En la segunda prueba, deben nombrar el color impreso (C) (rojo, azul o verde) de las letras XXX. En la tercera prueba, deben nombrar el color de la palabra impresa (rojo, azul o verde), que difiere de la palabra escrita (rojo, azul o verde) (PC). Consecutivamente, se calcula el índice PC' ((P x C) / (P + C)) y el índice de Interferencia Stroop (WC - WC ').

9.2.6 Cuestionarios

Las *quejas subjetivas de memoria* fueron evaluadas con la adaptación española (Lozoya-Delgado et al., 2012) del cuestionario MFE-30 (Sunderland et al., 1984). Se trata de un cuestionario de 30 ítems sobre situaciones y actividades de la vida diaria, valorados en una escala tipo Likert de 5 puntos que va de 0 (nunca o casi nunca) a 4 (siempre o casi siempre).

La *depresión* fue evaluada con el BDI-II (Beck et al., 1996). Este cuestionario consiste en 21 ítems sobre síntomas tales como tristeza, llanto, pérdida de placer, sentimientos de fracaso y de culpa, pensamientos o deseos de suicidio, pesimismo, etc, valorados en una escala tipo Likert que va de 0 a 3.

La reserva cognitiva fue evaluada con el Cuestionario de Reserva Cognitiva (CR; Rami et al., 2011). Este cuestionario consta de 8 ítems que miden actividad intelectual.

9.3 CONCLUSIONES

El primer objetivo de esta tesis fue examinar si el procesamiento de las emociones faciales positivas, negativas y neutras es diferente en jóvenes con y sin SMCs. Para esto se compararon datos comportamentales y ERPs. Los resultados, presentados en el capítulo 3**,** revelaron que los participantes jóvenes con SMCs mostraron amplitudes más bajas que los participantes sin SMCs en el componente N170, específicamente para caras positivas y neutras. Esta menor amplitud en N170 podría reflejar dificultades de procesamiento emocional en la etapa de codificación de la estructura facial donde se combinan procesos de abajo hacia arriba y la representación estructural de una cara se asocia con la información semántica necesaria para formar una representación interna de un rostro humano (Bentin et al., 1996; Sagiv & Bentin, 2001). Asimismo, este componente también participa en el procesamiento de emociones faciales, especialmente para el procesamiento temprano de la valencia emocional (Qiu et al., 2017). Por otro lado, la menor amplitud elicitada fue específica para las caras positivas y neutras mientras que las caras negativas produjeron la misma amplitud en ambos grupos. Desde un punto de vista biológico, esto podría tener una función adaptativa, dado que el reconocimiento de caras negativas es más relevante porque estas expresiones son signos de una amenaza potencial (Calvo & Beltrán, 2013).

Con respecto al componente LPP, no se encontraron diferencias entre los grupos ni en latencia ni en amplitud, lo cual indicaría que los jóvenes con SMCs no presentan dificultades en el procesamiento emocional tardío, lo que implica que la atención sostenida se encuentra preservada (Luo et al., 2010). Finalmente, observamos que los hombres mostraron amplitudes más pequeñas para los componentes N170 y LPP que las mujeres. En este sentido, varios estudios han investigado la relación entre el sexo y el procesamiento de emociones faciales, pero los resultados son inconsistentes (ver revisión: Herlitz & Lovén, 2013; Proverbio, 2017; Verhallen et al., 2017). Nuestro hallazgo sugiere que, en general, las mujeres muestran un

procesamiento atencional más sensible de las caras emocionales que los hombres iniciándose en la primera etapa y manteniéndose en el proceso evaluativo tardío.

El segundo objetivo de la presente tesis fue determinar si existen diferencias en los correlatos neuronales y medidas conductuales del procesamiento de emociones faciales y su relación con la EF, entre personas mayores con y sin SMCs. Para esto se utilizaron los datos de comportamiento y ERPs, tal y como han propuesto otros estudios llevados a cabo con personas con MCI and AD (Sarabia-Cobo et al., 2015; Schefter et al., 2013; Yang et al., 2015). Los resultados, presentados en el capítulo 4, indicaron que los participantes con SMCs tenían RT más largos y menos precisión en el procesamiento emocional facial que los participantes sin SMCs, lo cual está en línea con estudios previos (Pietschnig et al., 2015; Teng et al., 2007; Varjassyová et al., 2012).

Con respecto a los ERPs, los análisis revelaron diferencias de grupo sólo en el componente N170. En concreto, los hombres con SMCs mostraron latencias más largas que los hombres del grupo de control, además, los hombres con SMCs revelaron latencias más largas que las mujeres con SMCs. En esta línea solo un estudio exploró el papel del sexo en personas con SMCs (Pietschnig et al., 2015) demostrando, con datos conductuales, una fuerte desventaja en una tarea de reconocimiento de emociones faciales para los hombres con SMCs, en comparación con las mujeres, lo que podría ser consistente con nuestros hallazgos neuronales. Por lo tanto, las latencias prolongadas de N170 indican que la codificación de la estructura facial y el procesamiento emocional pueden ser más lentos en las personas mayores con SMCs, tal y como sucede en personas con MCI (Schefter et al., 2013; Yang et al., 2015). Por el contrario, para los componentes tardíos P300 y LPP no se encontraron diferencias ni en

latencias ni en amplitudes entre los participantes con y sin SMCs, lo cual indicaría que las fases tardías de procesamiento de caras emocionales se encuentran conservadas.

Con respecto a la posible asociación entre los ERPs y las EF, encontramos que amplitudes más altas de P300 y LPP para caras negativas versus neutras se asociaron con niveles más altos de memoria de trabajo verbal y visuoespacial y velocidad y atención psicomotora general. Estudios previos ya habían propuesto una interrelación entre el procesamiento de las emociones faciales con el funcionamiento ejecutivo (Ibáñez et al., 2011; Mathersul et al., 2009; Pessoa, 2009; Teng et al., 2007). Además, el aumento de amplitud para caras emocionales reflejaría un mayor esfuerzo cognitivo (Olofsson et al., 2008; Schupp et al., 2006). Finalmente, nuestros datos indican un mejor desempeño de las mujeres que de los hombres. Estos resultados respaldan y amplían la evidencia que muestra que las mujeres procesan la información afectiva significativamente mejor que los hombres (Campanella et al., 2004; Choi et al., 2015; Li et al., 2008).

El tercer objetivo de esta tesis fue investigar si los ritmos corticales del EEG en estado de reposo, habitualmente alterados en MCI y AD, también se ven afectados en las personas mayores y jóvenes con SMCs en comparación con las personas control. Los resultados expuestos en el capítulo 5 mostraron que las personas mayores con SMCs tuvieron un aumento en la potencia espectral de theta y una menor reactividad a los EO en la banda alpha comparados con los controles. El aumento de la potencia theta en mayores con SMCs se había descrito en estudios anteriores (Alexander et al., 2006; Gouw et al., 2017; Prichep et al., 1994). Desde un punto de vista fisiológico, las oscilaciones del EEG reflejan el acoplamiento de grupos locales de neuronas inhibitorias y neuronas piramidales excitatorias corticales (Biasiucci et al., 2019). Por lo tanto, una menor activación de estas neuronas por la interrupción

del procesamiento de la información en el sistema colinérgico puede conducir a un aumento en la potencia de theta (Jeong, 2004; Roh et al., 2011). Asimismo, la pérdida de reactividad EEG encontrada en alpha central podría estar asociada con esta alteración del sistema colinérgico ya que el ritmo alpha es modulado por la acetilcolina (Goldman et al., 2002). Además, aumentos en la potencia espectral de las bandas delta, theta y beta se correlacionaron con mejor desempeño en tareas de memoria verbal y EF. Similares asociaciones entre theta y memoria verbal y de trabajo han sido reportadas previamente (Alexander et al., 2006), así como una correlación entre el aumento de la potencia delta y un mejor desempeño en tareas de memoria verbal/visuoespacial, y funciones de producción del lenguaje en pacientes con MCI y AD (Babiloni et al., 2012).

Con respecto a los jóvenes no se encontraron diferencias entre los SMCs y los controles en ninguna banda de frecuencia ni en la reactividad del EEG. La ausencia de diferencias EEG entre grupos podría ser un indicador de que la actividad eléctrica del cerebro está relativamente preservada. Sin embargo, si se pudo ver una correlación con un efecto opuesto al encontrado en las personas mayores con SMCs, es decir, el aumento de la potencia espectral en theta y beta se relacionó con peor desempeño en memoria verbal y EF. Estos hallazgos sugieren que los cambios en el EEG pueden ser no lineales entre las personas jóvenes y mayores con SMCs.

El cuarto objetivo de esta tesis fue investigar si los principales parámetros del pico alpha, el APF y la amplitud, eran diferentes en personas con y sin SMCs, así como explorar los cambios de APF y amplitud relacionados con la edad y el sexo. Además, se estudió la relación entre CR y APF en personas con y sin SMCs en cada grupo de edad. Para ello, se registraron los datos del EEG en estado de reposo con los ojos cerrados durante tres minutos. Los resultados presentados en el capítulo 5 mostraron que no hubo diferencias ni en APF ni en la amplitud de alpha entre mayores y jóvenes con SMCs y el grupo control. Tampoco se detectaron diferencias significativas por sexo. Independientemente de la condición y el sexo,

replicamos los hallazgos previos de disminución de la amplitud en las personas mayores en comparación con las personas más jóvenes. Además, en las personas mayores con SMCs, una mayor CR se correlacionó significativamente con una APF más lenta. Por el contrario, en los jóvenes del grupo control, una mayor CR se correlacionó con mayor amplitud de Pz, P3 y O2. Aunque estudios previos han reportado una ralentización de la APF y disminución de la amplitud en MCI (Garcés et al., 2013) y una reducida APF en la AD (Ruiz-Gómez et al., 2018), la hipótesis de que los parámetros del pico de alpha de las SMCs son más lentos comparados con el grupo control no se confirmó en nuestra muestra. Los parámetros del pico de alpha no se determinan únicamente por la patología, sino que también dependen de otros factores como la edad o el sexo. Los adultos mayores y los jóvenes tenían un APF similar; en contraste, las amplitudes se redujeron significativamente en las personas mayores, especialmente en las regiones occipitales, lo que llevó a la conclusión de que, aunque no se observó una desaceleración del APF, la producción alpha podría verse comprometida en las personas mayores.

El patrón de resultados observado en este estudio proporciona un complemento importante a la literatura que informa de una alta estabilidad de APF y amplitud alpha a lo largo del tiempo en ausencia de patología, como lo muestran las personas sanas con SMCs. Esto sugiere que los cambios sustanciales en estos parámetros podrían ser indicativos de un proceso patológico, como la progresión de la enfermedad (Babiloni et al., 2009). Además, la relación entre APF y CR encontrada en este estudio en personas mayores con SMCs podría revelar un mecanismo compensatorio de la CR sobre los mecanismos que modulan los ritmos alpha. Por lo tanto, estos parámetros alpha podrían ser buenos candidatos para monitorear las desviaciones de la función cerebral normal.

REFERENCES

Abdulrab, K., & Heun, R. (2008). Subjective Memory Impairment. A review of its definitions indicates the need for a comprehensive set of standardised and validated criteria. *European Psychiatry*, *23*(5), 321–330. https://doi.org/10.1016/j.eurpsy.2008.02.004

Adler, N. E., Epel, E. S., Castellazzo, G., & Ickovics, J. R. (2000). Relationship of subjective and objective social status with psychological and physiological functioning: Preliminary data in healthy white women. *Health Psychology*, *19*(6), 586–592. https://doi.org/10.1037/0278-6133.19.6.586

Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology*, *12*(2), 169–177. https://doi.org/10.1016/s0959-4388(02)00301-x

Alexander, d. M., Arns, M. W., Paul, R. H., Rowe, D. L., Cooper, N., Esser, A. H., Fallahpour, K., Stephan, B. C. M., Heesen, E., Breteler, R., Williams, L. M., & Gordon, E. (2006). EEG markers for cognitive decline in elderly subjects with subjective memory complaints. *journal of integrative neuroscience*, *5*(1), 49–74. https://doi.org/10.1142/s0219635206001021

Alloway, T. P., Gathercole, S. E., Kirkwood, H., & Elliott, J. (2008). Evaluating the validity of the Automated Working Memory Assessment. *Educational Psychology*, *28*(7), 725–734. https://doi.org/10.1080/01443410802243828

Asaumi, Y., Morita, K., Nakashima, Y., Muraoka, A., & Uchimura, N. (2014). Evaluation of P300 components for emotion-loaded visual event-related potential in elderly subjects, including those with dementia. *Psychiatry and Clinical Neurosciences*, *68*(7), 558–567. https://doi.org/10.1111/pcn.12162

Aurlien, H., Gjerde, I. O., Aarseth, J. H., Eldøen, G., Karlsen, B., Skeidsvoll, H., & Gilhus, N. E. (2004). EEG background activity described by a large computerized database. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *115*(3), 665–673. https://doi.org/10.1016/J.CLINPH.2003.10.019

Babiloni, C., Barry, R. J., Başar, E., Blinowska, K. J., Cichocki, A., Drinkenburg, W. H., Klimesch, W., Knight, R. T., Silva, F. L., Nunez, P., Oostenveld, R., Jeong, J., Pascual-Marqui, R., Valdes-Sosa, P., & Hallett, M. (2020a). International Federation of Clinical Neurophysiology (IFCN) – EEG research workgroup: Recommendations on frequency and topographic analysis of resting state EEG rhythms. Part 1: Applications in clinical research studies. *Clinical Neurophysiology*, *131*(1), 285–307. https://doi.org/10.1016/j.clinph.2019.06.234

Babiloni, C., Binetti, G., Cassarino, A., Dal Forno, G., Del Percio, C., Ferreri, F., Ferri, R., Frisoni, G., Galderisi, S., Hirata, K., Lanuzza, B., Miniussi, C., Mucci, A., Nobili, F., Rodriguez, G., Luca Romani, G., & Rossini, P. M. (2006). Sources of cortical rhythms in adults during physiological aging: A multicentric EEG study. *Human Brain Mapping*, *27*(2), 162–172. https://doi.org/10.1002/hbm.20175

Babiloni, C., Carducci, F., Lizio, R., Vecchio, F., Baglieri, A., Bernardini, S., Cavedo, E., Bozzao, A., Buttinelli, C., Esposito, F., Giubilei, F., Guizzaro, A., Marino, S., Montella, P., Quattrocchi, C. C., Redolfi, A., Soricelli, A., Tedeschi, G., Ferri, R., … Frisoni, G. B. (2012). Resting state cortical electroencephalographic rhythms are related to gray matter volume in subjects with mild cognitive impairment and Alzheimer's disease. *Human Brain Mapping*, *34*(6), 1427–1446. https://doi.org/10.1002/hbm.22005

Babiloni, C., Lizio, R., Marzano, N., Capotosto, P., Soricelli, A., Triggiani, A. I., Cordone, S., Gesualdo, L., & Del Percio, C. (2016). Brain neural synchronization and functional coupling in Alzheimer's disease as revealed by resting state EEG rhythms. *International Journal of Psychophysiology*, *103*(0), 88–102. https://doi.org/10.1016/j.ijpsycho.2015.02.008

Babiloni, C., Lopez, S., del Percio, C., Noce, G., Pascarelli, M. T., Lizio, R., Teipel, S. J., González-Escamilla, G., Bakardjian, H., George, N., Cavedo, E., Lista, S., Chiesa, P. A., Vergallo, A., Lemercier, P., Spinelli, G., Grothe, M. J., Potier, M. C., Stocchi, F., … Hampel, H. (2020b). Resting-state posterior alpha rhythms are abnormal in subjective memory complaint seniors with preclinical Alzheimer's neuropathology and high education level: the INSIGHT-preAD study. *Neurobiology of Aging*, *90*, 43–59. https://doi.org/10.1016/J.NEUROBIOLAGING.2020.01.012

Babiloni, C., Pievani, M., Vecchio, F., Geroldi, C., Eusebi, F., Fracassi, C., Fletcher, E., de Carli, C., Boccardi, M., Rossini, P. M., & Frisoni, G. B. (2009). White-matter lesions along the cholinergic tracts are related to cortical sources of EEG rhythms in amnesic mild cognitive impairment. *Human Brain Mapping*, *30*(5), 1431. https://doi.org/10.1002/HBM.20612

Babiloni, C., Visser, P. J., Frisoni, G., Deyn, P. P. D., Bresciani, L., Jelic, V., Nagels, G., Rodriguez, G., Rossini, P. M., Vecchio, F., Colombo, D., Verhey, F., Wahlund, L. O., & Nobili, F. (2010). Cortical sources of resting EEG rhythms in mild cognitive impairment and subjective memory complaint. *Neurobiology of Aging*, *31*(10), 1787–1798. https://doi.org/10.1016/j.neurobiolaging.2008.09.020

Balash, Y., Mordechovich, M., Shabtai, H., Giladi, N., Gurevich, T., & Korczyn, A. D. (2012). Subjective memory complaints in elders: depression, anxiety, or cognitive decline? *Acta Neurologica Scandinavica*, *127*(5), 344–350. https://doi.org/10.1111/ane.12038

Barry, R. J., & De Blasio, F. M. (2017). EEG differences between eyes-closed and eyes-open resting remain in healthy ageing. *Biological Psychology*, *129*(0), 293–304. https://doi.org/10.1016/j.biopsycho.2017.09.010

Bartussek, D., Becker, G., Diedrich, O., Naumann, E., & Maier, S. (1996). Extraversion, neuroticism, and event-related brain potentials in response to emotional stimuli. *Personality and Individual Differences*, *20*(3), 301–312. https://doi.org/10.1016/0191-8869(95)00175-1

Başar, E., Başar-Eroglu, C., Karakaş, S., & Schürmann, M. (2001). Gamma, alpha, delta, and theta oscillations govern cognitive processes. *International Journal of Psychophysiology*, *39*(2), 241–248. https://doi.org/10.1016/s0167-8760(00)00145-8

Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. (1996). Comparison of beck depression inventories -IA and -II in psychiatric outpatients. *Journal of Personality Assessment*, 67, 588– 597. https://doi.org/10.1037/t00742-000

Begum, A., Dewey, M., Hassiotis, A., Prince, M., Wessely, S., & Stewart, R. (2013). Subjective cognitive complaints across the adult life span: a 14-year analysis of trends and associations using the 1993, 2000 and 2007 English Psychiatric Morbidity Surveys. *Psychological Medicine*, *44*(9), 1977–1987. https://doi.org/10.1017/s0033291713002444

Benito-León, J., Mitchell, A. J., Vega, S., & Bermejo-Pareja, F. (2010). A population-based study of cognitive function in older people with subjective memory complaints. *Journal of Alzheimer's Disease*, **22**(1), 159– 170. https://doi.org/10.3233/JAD-2010-100972

Bentin, S., Allison, T., Puce, A., Perez, E., & McCarthy, G. (1996). Electrophysiological Studies of Face Perception in Humans. *Journal of Cognitive Neuroscience*, *8*(6), 551–565. https://doi.org/10.1162/jocn.1996.8.6.551

Biasiucci, A., Franceschiello, B., & Murray, M. M. (2019). Electroencephalography. *Current Biology*, *29*(3), R80–R85. https://doi.org/10.1016/j.cub.2018.11.052

Blau, V. C., Maurer, U., Tottenham, N., & McCandliss, B. D. (2007). The face-specific N170 component is modulated by emotional facial expression. *Behavioral and Brain Functions*, *3*(1), 1–13. https://doi.org/10.1186/1744-9081-3-7/TABLES/1

Bora, E., & Yener, G. G. (2017). Meta-Analysis of Social Cognition in Mild Cognitive Impairment. *Journal of Geriatric Psychiatry and Neurology*, *30*(4), 206–213. https://doi.org/10.1177/0891988717710337

Bradley, M. M. (2009). Natural selective attention: Orienting and emotion. *Psychophysiology*, *46*(1), 1–11. https://doi.org/10.1111/j.1469-8986.2008.00702.x

Brailean, A., Steptoe, A., Batty, G. D., Zaninotto, P., & Llewellyn, D. J. (2019). Are subjective memory complaints indicative of objective cognitive decline or depressive symptoms? Findings from the English Longitudinal Study of Ageing. *Journal of Psychiatric Research*, *110*(0), 143–151. https://doi.org/10.1016/j.jpsychires.2018.12.005

Burmester, B., Leathem, J., & Merrick, P. (2016). Subjective Cognitive Complaints and Objective Cognitive Function in Aging: A Systematic Review and Meta-Analysis of Recent Cross-Sectional Findings. *Neuropsychology Review*, *26*(4), 376–393. https://doi.org/10.1007/s11065-016-9332-2

Burmester, B., Leathem, J., & Merrick, P. (2015). Assessing subjective memory complaints: A comparison of spontaneous reports and structured questionnaire methods. *International Psychogeriatrics*, 27(1), 61– 77. https://doi.org/10.1017/S1041610214001161

Caharel, S., Leleu, A., Bernard, C., Viggiano, M. P., Lalonde, R., & Rebaï, M. (2013). Early holistic face-like processing of Arcimboldo paintings in the right occipito-temporal cortex: Evidence from the N170 ERP component. *International Journal of Psychophysiology*, *90*(2), 157–164. https://doi.org/10.1016/j.ijpsycho.2013.06.024

Calvo, M. G., & Beltrán, D. (2013). Recognition advantage of happy faces: Tracing the neurocognitive processes. *Neuropsychologia*, *51*(11), 2051–2061. https://doi.org/10.1016/j.neuropsychologia.2013.07.010

Calvo, M. G., & Lundqvist, D. (2008). Facial expressions of emotion (KDEF): Identification under different display-duration conditions. *Behavior Research Methods 2008 40:1*, *40*(1), 109–115. https://doi.org/10.3758/BRM.40.1.109

Campanella, S., Rossignol, M., Mejias, S., Joassin, F., Maurage, P., Debatisse, D., Bruyer, R., Crommelinck, M., & Guérit, J. (2004). Human gender differences in an emotional visual oddball task: an event-related potentials study. *Neuroscience Letters*, *367*(1), 14–18. https://doi.org/10.1016/j.neulet.2004.05.097

Cantero, J. L., Iglesias, J. E., Van Leemput, K., & Atienza, M. (2016). Regional Hippocampal Atrophy and Higher Levels of Plasma Amyloid-Beta Are Associated With Subjective Memory Complaints in Nondemented Elderly Subjects. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *71*(9), 1210–1215. https://doi.org/10.1093/gerona/glw022

Carstensen, L., Mikels, J. A., & Mather, M. (2006). Aging and the intersection of cognition, motivation, and emotion. In K. S. James Birren (Ed.), *Handbook of the psychology of aging* (Vol. **6**, pp. 343– 362). Elsevier.

Cave, A. E., & Barry, R. J. (2021). Sex differences in resting EEG in healthy young adults. *International Journal of Psychophysiology*, *161*(0), 35–43. https://doi.org/10.1016/j.ijpsycho.2021.01.008

Cespón, J., Galdo-Álvarez, S., & Díaz Fernando. (2018). Event-Related Potentials Reveal Altered Executive Control Activity in Healthy Elderly With Subjective Memory Complaints. *Frontiers in Human Neuroscience*, *12*. https://doi.org/10.3389/fnhum.2018.00445

Chae, S., Park, J., Byun, M. S., Yi, D., Lee, J. H., Byeon, G. H., Suk, H. W., Choi, H., Park, J. E., & Lee, D. Y. (2020). Decreased Alpha Reactivity from Eyes-Closed to Eyes-Open in Non-Demented Older Adults with Alzheimer's Disease: A Combined EEG and [18F]florbetaben PET Study. *Journal of Alzheimer's Disease*, *77*(4), 1681–1692. https://doi.org/10.3233/jad-200442

Cherubini, A., Péran, P., Caltagirone, C., Sabatini, U., & Spalletta, G. (2009). Aging of subcortical nuclei: microstructural, mineralization and atrophy modifications measured in vivo using MRI. *NeuroImage*, *48*(1), 29–36. https://doi.org/10.1016/J.NEUROIMAGE.2009.06.035

Chiang, A. K. I., Rennie, C. J., Robinson, P. A., van Albada, S. J., & Kerr, C. C. (2011). Age trends and sex differences of alpha rhythms including split alpha peaks. *Clinical Neurophysiology*, *122*(8), 1505–1517. https://doi.org/10.1016/J.CLINPH.2011.01.040

Choi, D., Egashira, Y., Takakura, J., Motoi, M., Nishimura, T., & Watanuki, S. (2015). Gender difference in N170 elicited under oddball task. *Journal of Physiological Anthropology*, *34*(1). https://doi.org/10.1186/s40101-015-0045-7

Churches, O., Nicholls, M., Thiessen, M., Kohler, M., & Keage, H. (2014). Emoticons in mind: An event-related potential study. *Social Neuroscience*, *9*(2), 196–202. https://doi.org/10.1080/17470919.2013.873737

Collignon, O., Girard, S., Gosselin, F., Saint-Amour, D., Lepore, F., & Lassonde, M. (2010). Women process multisensory emotion expressions more efficiently than men. *Neuropsychologia*, 48(1), 220– 225. https://doi.org/10.1016/j.neuropsychologia.2009.09.007

Conklin, H. M., Curtis, C. E., Katsanis, J., & Iacono, W. G. (2000). Verbal working memory impairment in schizophrenia patients and their first-degree relatives: Evidence from the digit span task. *American Journal of Psychiatry*, 157(2), 275– 277. https://doi.org/10.1176/appi.ajp.157.2.275

Constantinidou, F., Zaganas, I., Papastefanakis, E., Kasselimis, D., Nidos, A., & Simos, P. G. (2014). Age-Related Decline in Verbal Learning Is Moderated by Demographic Factors, Working Memory Capacity, and Presence of Amnestic Mild Cognitive Impairment. *Journal of the International Neuropsychological Society*, *20*(8), 822–835. https://doi.org/10.1017/S1355617714000678

Cristofori, I., Cohen-Zimerman, S., & Grafman, J. (2019). Executive functions. *Handbook of Clinical Neurology*, *0*(0), 197–219. https://doi.org/10.1016/b978-0-12-804281-6.00011-2

Crumley, J. J., Stetler, C. A., & Horhota, M. (2014). Examining the relationship between subjective and objective memory performance in older adults: A meta-analysis. *Psychology and Aging*, *29*(2), 250–263. https://doi.org/10.1037/a0035908

Cummins, T. D., & Finnigan, S. (2007). Theta power is reduced in healthy cognitive aging. *International Journal of Psychophysiology*, *66*(1), 10–17. https://doi.org/10.1016/j.ijpsycho.2007.05.008

Cuthbert, B. N., Schupp, H. T., Bradley, M. M., Birbaumer, N., & Lang, P. J. (2000). Brain potentials in affective picture processing: covariation with autonomic arousal and affective report. *Biological Psychology*, *52*(2), 95–111. https://doi.org/10.1016/s0301-0511(99)00044-7

Derouesné, C., Lacomblez, L., Thibault, S., & Leponcin, M. (1999). Memory complaints in young and elderly subjects. *International journal of geriatric psychiatry*, *14*(4), 291-301.

Dugdale, D. E. (1993). Essentials of electromagnetism. New York, NY: American Institute of Physics

Eimer, M. (2000). The face-specific N170 component reflects late stages in the structural encoding of faces. *Neuroreport*, *11*(10), 2319–2324.

Eimer, M. (2000). Event-related brain potentials distinguish processing stages involved in face perception and recognition. *Clinical Neurophysiology*, 111(4), 694– 705. https://doi.org/10.1016/S1388-2457(99)00285-0

Eimer, M., & Holmes, A. (2007). Event-related brain potential correlates of emotional face processing. *Neuropsychologia*, *45*(1), 15–31. https://doi.org/10.1016/j.neuropsychologia.2006.04.022

Elferink, M. W., Tilborg, I., & Kessels, R. P. (2015). Perception of emotions in mild cognitive impairment and Alzheimer's dementia: does intensity matter? *Translational Neuroscience*, *6*(1). https://doi.org/10.1515/tnsci-2015-0013

Engel, A. K., & Fries, P. (2010). Beta-band oscillations—signalling the status quo? *Current Opinion in Neurobiology*, *20*(2), 156–165. https://doi.org/10.1016/j.conb.2010.02.015

Fernández, A., Hornero, R., Mayo, A., Poza, J., Gil-Gregorio, P., & Ortiz, T. (2006). MEG spectral profile in Alzheimer's disease and mild cognitive impairment. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *117*(2), 306–314. https://doi.org/10.1016/J.CLINPH.2005.10.017

Fide, E., Emek-Savaş, D. D., Aktürk, T., Güntekin, B., Hanoğlu, L., & Yener, G. G. (2019). Electrophysiological evidence of altered facial expressions recognition in Alzheimer's disease: A comprehensive ERP study. *Clinical Neurophysiology*, 130(10), 1813– 1824. https://doi.org/10.1016/j.clinph.2019.06.229

Fonseca, L. C., Tedrus, G. M. A. S., Fondello, M. A., Reis, I. N., & Fontoura, D. S. (2011). EEG Theta and Alpha Reactivity on Opening the Eyes in the Diagnosis of Alzheimer's Disease. *Clinical EEG and Neuroscience*, *42*(3), 185–189. https://doi.org/10.1177/155005941104200308

Fröhlich, S., Kutz, D. F., Müller, K., & Voelcker-Rehage, C. (2021). Characteristics of Resting State EEG Power in 80+-Year-Olds of Different Cognitive Status. *Frontiers in Aging Neuroscience*, *13*(469). https://doi.org/10.3389/fnagi.2021.675689

Galluzzi, S., & Frisoni, G. B. (2008). Imaging, subjective complaints, and MCI: 30 years before. *The Journal of Nutrition Health and Aging*, *12*(0), S80–S83. https://doi.org/10.1007/bf02982592

Garcés, P., Vicente, R., Wibral, M., Pineda-Pardo, J. ángel, López, M. E., Aurtenetxe, S., Marcos, A., de Andrés, M. E., Yus, M., Sancho, M., Maestú, F., & Fernández, A. (2013). Brain-wide slowing of spontaneous alpha rhythms in mild cognitive impairment. *Frontiers in Aging Neuroscience*, *5*(DEC), 100. https://doi.org/10.3389/FNAGI.2013.00100/BIBTEX

Garrido-Chaves, R., Perez, V., Perez-Alarcón, M., Crespo-Sanmiguel, I., Paiva, T. O., Hidalgo, V., Pulopulos, M., & Salvador, A. (2021). Subjective Memory Complaints and Decision Making in Young and Older Adults: An Event-Related Potential Study. *Frontiers in Aging Neuroscience*, *13*. https://doi.org/10.3389/fnagi.2021.695275

Gaubert, S., Raimondo, F., Houot, M., Corsi, M. C., Naccache, L., Diego Sitt, J., Hermann, B., Oudiette, D., Gagliardi, G., Habert, M. O., Dubois, B., De Vico Fallani, F., Bakardjian, H., & Epelbaum, S. (2019). EEG evidence of compensatory mechanisms in preclinical Alzheimer's disease. *Brain*, *142*(7), 2096–2112. https://doi.org/10.1093/brain/awz150

Genziani, M., Stewart, R., Béjot, Y., Amieva, H., Artero, S., & Ritchie, K. (2012). Subjective memory impairment, objective cognitive functioning and social activity in French older people: Findings from the Three Cities study. *Geriatrics & Gerontology International*, *13*(1), 139–145. https://doi.org/10.1111/j.1447-0594.2012.00873.x

Ghazi, T. R., Blacker, K. J., Hinault, T. T., & Courtney, S. M. (2021). Modulation of Peak Alpha Frequency Oscillations During Working Memory Is Greater in Females Than Males. *Frontiers in Human Neuroscience*, *15*, 192. https://doi.org/10.3389/FNHUM.2021.626406/BIBTEX

Ginó, S., Mendes, T., Maroco, J., Ribeiro, F., Schmand, B. A., Mendonça, A., & Guerreiro, M. (2010). Memory Complaints Are Frequent but Qualitatively Different in Young and Elderly Healthy People. *Gerontology*, *56*(3), 272–277. https://doi.org/10.1159/000240048

Gironell, A., Garcia-Sanchez, C., Estvez-Gonzalez, A., Boltes, A., & Kulisevsky, J. (2005). Usefulness of P300 in subjective memory complaints. *Journal of Clinical Neurophysiology*, 22(4), 279– 284. https://doi.org/10.1097/01.wnp.0000173559.60113.ab

Glodzik-Sobanska, L., Reisberg, B., De Santi, S., Babb, J. S., Pirraglia, E., Rich, K. E., Brys, M., & Leon, M. J. (2007). Subjective Memory Complaints: Presence, Severity and Future Outcome in Normal Older Subjects. *Dementia and Geriatric Cognitive Disorders*, *24*(3), 177–184. https://doi.org/10.1159/000105604

Golden, C. J. (1978). A manual for the clinical and experimental use of the stroop color and word test. Stoelting Company.

Goldman, R. I., Stern, J. M., Engel, J., & Cohen, M. S. (2002). Simultaneous EEG and fMRI of the alpha rhythm. *NeuroReport*, *13*(18), 2487–2492. https://doi.org/10.1097/00001756-200212200-00022

Gouveia, P. A. R., Brucki, S. M. D., Malheiros, S. M. F., & Bueno, O. F. A. (2007). Disorders in planning and strategy application in frontal lobe lesion patients. *Brain and Cognition*, 63(3), 240– 246. https://doi.org/10.1016/j.bandc.2006.09.001

Gouw, A. A., Alsema, A. M., Tijms, B. M., Borta, A., Scheltens, P., Stam, C. J., & Flier, W. M. (2017). EEG spectral analysis as a putative early prognostic biomarker in nondemented, amyloid positive subjects. *Neurobiology of Aging*, *57*(0), 133–142. https://doi.org/10.1016/j.neurobiolaging.2017.05.017

Grandy, T. H., Werkle-Bergner, M., Chicherio, C., Lövdén, M., Schmiedek, F., & Lindenberger, U. (2013a). Individual alpha peak frequency is related to latent factors of general cognitive abilities. *NeuroImage*, *79*, 10–18. https://doi.org/10.1016/J.NEUROIMAGE.2013.04.059

Grandy, T. H., Werkle-Bergner, M., Chicherio, C., Schmiedek, F., Lövdén, M., & Lindenberger, U. (2013b). Peak individual alpha frequency qualifies as a stable neurophysiological trait marker in healthy younger and older adults. *Psychophysiology*, *50*(6), 570–582. https://doi.org/10.1111/PSYP.12043

Gratton, G., Coles, M. G. H., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, *55*(4), 468–484. https://doi.org/10.1016/0013-4694(83)90135-9

Gur, R. C., Sara, R., Hagendoorn, M., Marom, O., Hughett, P., Macy, L., Turner, T., Bajcsy, R., Posner, A., & Gur, R. E. (2002). A method for obtaining 3-dimensional facial expressions and its standardization for use in neurocognitive studies. *Journal of Neuroscience Methods*, *115*(2), 137–143. https://doi.org/10.1016/s0165-0270(02)00006-7

Hafkemeijer, A., Altmann-Schneider, I., Oleksik, A. M., Wiel, L., Middelkoop, H. A., Buchem, M. A., Grond, J., & Rombouts, S. A. (2013). Increased Functional Connectivity and Brain Atrophy in Elderly with Subjective Memory Complaints. *Brain Connectivity*, *3*(4), 353–362. https://doi.org/10.1089/brain.2013.0144

Hajcak, G., & Foti, D. (2020). Significance?... Significance! Empirical, methodological, and theoretical connections between the late positive potential and P300 as neural responses to stimulus significance: An integrative review. *Psychophysiology*, *57*(7). https://doi.org/10.1111/psyp.13570

Hampson, E., Vananders, S.M, & Mullin, L. (2006). A female advantage in the recognition of emotional facial expressions: test of an evolutionary hypothesis. *Evolution and Human Behavior*, *27*(6), 401–416. https://doi.org/10.1016/j.evolhumbehav.2006.05.002

Hatz, F., Benz, N., Hardmeier, M., Zimmermann, R., Rueegg, S., Schindler, C., Miserez, A., Gschwandtner, U., Monsch, A., & Fuhr, P. (2013). Quantitative EEG and apolipoprotein E-genotype improve classification of patients with suspected Alzheimer's disease. *Clinical Neurophysiology*, *124*(11), 2146–2152. https://doi.org/10.1016/j.clinph.2013.04.339

Herlitz, A., & Lovén, J. (2014). Sex differences and the own-gender bias in face recognition: A meta-analytic review. *Visual Cognition*, *21*(9), 1306–1336. https://doi.org/10.1080/13506285.2013.823140

Hinojosa, J., Mercado, F., & Carretié, L. (2015). N170 sensitivity to facial expression: A meta-analysis. *Neuroscience & Biobehavioral Reviews*, *55*, 498–509. https://doi.org/10.1016/j.neubiorev.2015.06.002

Hohman, T. J., Beason-Held, L. L., Lamar, M., & Resnick, S. M. (2011). Subjective cognitive complaints and longitudinal changes in memory and brain function. *Neuropsychology*, *25*(1), 125–130. https://doi.org/10.1037/a0020859

Holmen, J., Langballe, E. M., Midthjell, K., Holmen, T. L., Fikseaunet, A., Saltvedt, I., & Tambs, K. (2013). Gender differences in subjective memory impairment in a general population: the HUNT study, Norway. *BMC Psychology*, *1*(1). https://doi.org/10.1186/2050-7283-1-19

Holmes, A., Winston, J. S., & Eimer, M. (2005). The role of spatial frequency information for ERP components sensitive to faces and emotional facial expression. *Cognitive Brain Research*, *25*(2), 508–520. https://doi.org/10.1016/j.cogbrainres.2005.08.003

Holmes, G. L., & Khazipov, R. (2007). Basic Neurophysiology and the Cortical Basis of EEG. *The Clinical Neurophysiology Primer*, *0*(0), 19–33. https://doi.org/10.1007/978-1-59745-271-7_2

Ibáñez, A., Petroni, A., Urquina, H., Torrente, F., Torralva, T., Hurtado, E., Guex, R., Blenkmann, A., Beltrachini, L., Muravchik, C., Baez, S., Cetkovich, M., Sigman, M., Lischinsky, A., & Manes, F. (2011). Cortical deficits of emotional face processing in adults with ADHD: Its relation to social cognition and executive function. *Social Neuroscience*, *6*(5), 464–481. https://doi.org/10.1080/17470919.2011.620769

Iliffe, S., & Pealing, L. (2010). Subjective memory problems. *BMJ (Clinical Research Ed.)*, *340*(7748), 703–706. https://doi.org/10.1136/BMJ.C1425

Jackson, A. F., & Bolger, D. J. (2014). The neurophysiological bases of EEG and EEG measurement: A review for the rest of us. *Psychophysiology*, *51*(11), 1061–1071. https://doi.org/10.1111/psyp.12283

Jacob, L., Haro, J. M., & Koyanagi, A. (2019). Physical multimorbidity and subjective cognitive complaints among adults in the United Kingdom: a cross-sectional community-based study. *Scientific Reports*, *9*(1). https://doi.org/10.1038/s41598-019-48894-8

Jeong, J. (2004). EEG dynamics in patients with Alzheimer's disease. *Clinical Neurophysiology*, *115*(7), 1490–1505. https://doi.org/10.1016/j.clinph.2004.01.001

Jessen, F. (2020). Attention in subjective cognitive decline – Authors' reply. *The Lancet Neurology*, *19*(7), 566–567. https://doi.org/10.1016/s1474-4422(20)30177-0

Jessen, F., Amariglio, R. E., Boxtel, M., Breteler, M., Ceccaldi, M., Chételat, G., Dubois, B., Dufouil, C., Ellis, K. A., Flier, W. M., Glodzik, L., Harten, A. C., Leon, M. J., McHugh, P., Mielke, M. M., Molinuevo, J. L., Mosconi, L., Osorio, R. S., Perrotin, A., … and, M. W. (2014). A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & Dementia*, *10*(6), 844–852. https://doi.org/10.1016/j.jalz.2014.01.001

Jessen, F., Wiese, B., Bachmann, C., Eifflaender-Gorfer, S., Haller, F., Kölsch, H., & Wollny, A. (2010). Prediction of dementia by subjective memory impairment: Effects of severity and temporal association with cognitive impairment. *Archives of General Psychiatry*, 67(4), 414– 422. https://doi.org/10.1001/archgenpsychiatry.2010.30

Jones, R. N., Manly, J., Glymour, M. M., Rentz, D. M., Jefferson, A. L., & Stern, Y. (2011). Conceptual and Measurement Challenges in Research on Cognitive Reserve. *Journal of the International Neuropsychological Society*, *17*(4), 593–601. https://doi.org/10.1017/S1355617710001748

Joyce, C., & Rossion, B. (2005). The face-sensitive N170 and VPP components manifest the same brain processes: the effect of reference electrode site. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *116*(11), 2613–2631. https://doi.org/10.1016/J.CLINPH.2005.07.005

Juan, S. M. A., & Adlard, P. A. (2019). Ageing and Cognition. *Biochemistry and Cell Biology of Ageing: Part II Clinical Science*, *0*(0), 107–122. https://doi.org/10.1007/978-981-13-3681-2_5

Keil, A., Debener, S., Gratton, G., Junghöfer, M., Kappenman, E. S., Luck, S. J., Luu, P., Miller, G. A., & Yee, C. M. (2013). Committee report: Publication guidelines and recommendations for studies using electroencephalography and magnetoencephalography. *Psychophysiology*, *51*(1), 1–21. https://doi.org/10.1111/psyp.12147

Kenney, J. P. M., Ward, C., Gallen, D., Roche, R. A. P., Dockree, P., Hohensen, N., Cassidy, C., Keane, M. A., & Hogan, M. J. (2019). Self-initiated learning reveals memory performance and electrophysiological differences between younger, older and older adults with relative memory impairment. *European Journal of Neuroscience*, 50(11), 3855– 3872. https://doi.org/10.1111/ejn.14530

Kim, J., Kang, M. S., Cho, Y. S., & Lee, S. H. (2017). Prolonged Interruption of Cognitive Control of Conflict Processing Over Human Faces by Task-Irrelevant Emotion Expression. *Frontiers in Psychology*, *8*. https://doi.org/10.3389/fpsyg.2017.01024

Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews*, *29*(2), 169–195. https://doi.org/10.1016/s0165-0173(98)00056-3

Klimesch, W., Freunberger, R., Sauseng, P., & Gruber, W. (2008). A short review of slow phase synchronization and memory: Evidence for control processes in different memory systems? *Brain Research*, *1235*(0), 31–44. https://doi.org/10.1016/j.brainres.2008.06.049

Labouvie-Vief, G. (2003). Dynamic integration: Affect, cognition, and the self in adulthood. *Current Directions in Psychological Science*, 12(6), 201– 206. https://doi.org/10.1046/j.0963-7214.2003.01262.x

Lawrence, K., Campbell, R., & Skuse, D. (2015). Age, gender, and puberty influence the development of facial emotion recognition. *Frontiers in Psychology*, 6, 761. https://doi.org/10.3389/fpsyg.2015.00761

Lazarou, I., Adam, K., Georgiadis, K., Tsolaki, A., Nikolopoulos, S., Kompatsiaris, I. (yiannis), & Tsolaki, M. (2018). Can a Novel High-Density EEG Approach Disentangle the Differences of Visual Event Related Potential (N170), Elicited by Negative Facial Stimuli, in People with Subjective Cognitive Impairment? *Journal of Alzheimer's Disease*, *65*(2), 543–575. https://doi.org/10.3233/JAD-180223

Lee, S. D., Ong, B., Pike, K. E., & Kinsella, G. J. (2017). Prospective memory and subjective memory decline: A neuropsychological indicator of memory difficulties in community-dwelling older people. *Journal of Clinical and Experimental Neuropsychology*, *40*(2), 183–197. https://doi.org/10.1080/13803395.2017.1326465

Lejko, N., Larabi, D. I., Herrmann, C. S., Aleman, A., & Ćurčić-Blake, B. (2020). Alpha Power and Functional Connectivity in Cognitive Decline: A Systematic Review and Meta-Analysis. *Journal of Alzheimer's Disease*, *78*(3), 1047–1088. https://doi.org/10.3233/jad-200962

Leleu, A., Caharel, S., Carré, J., Montalan, B., Snoussi, M., Vom Hofe, A., Charvin, H., Lalonde, R., & Rebaï, M. (2010). Perceptual interactions between visual processing of facial familiarity and emotional expression: An event-related potentials study during task-switching. *Neuroscience Letters*, 482(2), 106– 111. https://doi.org/10.1016/j.neulet.2010.07.008

León, J. M., Llanero Luque, M., Lozoya Delgado, P., Fernández Blázquez, M. Á., & Pedrero Pérez, E. J. (2010). Estudio neuropsicológico de adultos jóvenes con quejas subjetivas de memoria: implicación de las funciones ejecutivas y otra sintomatología frontal asociada. *Revista De Neurología*, *51*(11), 650. https://doi.org/10.33588/rn.5111.2010270

Li, H., Yuan, J., & Lin, C. (2008). The neural mechanism underlying the female advantage in identifying negative emotions: An event-related potential study. *NeuroImage*, *40*(4), 1921–1929. https://doi.org/10.1016/j.neuroimage.2008.01.033

Liu, Y., Cai, Z. L., Xue, S., Zhou, X., & Wu, F. (2013). Proxies of cognitive reserve and their effects on neuropsychological performance in patients with mild cognitive impairment. *Journal of Clinical Neuroscience*, *20*(4), 548–553. https://doi.org/10.1016/j.jocn.2012.04.020

Lodder, S. S., & Putten, M. J. (2011). Automated EEG analysis: Characterizing the posterior dominant rhythm. *Journal of Neuroscience Methods*, *200*(1), 86–93. https://doi.org/10.1016/j.jneumeth.2011.06.008

Lojo-Seoane, C., Facal, D., Guàrdia-Olmos, J., & Juncos-Rabadán, O. (2014). Structural model for estimating the influence of cognitive reserve on cognitive performance in adults with subjective memory complaints. *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists*, *29*(3), 245–255. https://doi.org/10.1093/ARCLIN/ACU007

Lojo-Seoane, C., Facal, D., Guàrdia-Olmos, J., Pereiro, A. X., & Juncos-Rabadán, O. (2018). Effects of Cognitive Reserve on Cognitive Performance in a Follow-Up Study in Older Adults With Subjective Cognitive

Complaints. The Role of Working Memory. *Frontiers in Aging Neuroscience*, *10*, 189. https://doi.org/10.3389/FNAGI.2018.00189/BIBTEX

López-Sanz, D., Bruña, R., Garcés, P., Camara, C., Serrano, N., Rodríguez-Rojo I. C., Delgado, M. L., Montenegro, M., López-Higes, R., Yus, M., & Maestú, F. (2016). Alpha band disruption in the AD-continuum starts in the Subjective Cognitive Decline stage: a MEG study. *Scientific Reports*, *6*(1). https://doi.org/10.1038/srep37685

Loprinzi, P. (2019). Interrelationships between depression, exercise and subjective memory complaints. *Revue Neurologique*, *175*(5), 319–323. https://doi.org/10.1016/j.neurol.2018.10.006

Lozoya-Delgado, P., Ruiz-Sánchez de León, J. M., & Pedrero-Pérez, E. J. (2012). Validación de un cuestionario de quejas cognitivas para adultos jóvenes: relación entre las quejas subjetivas de memoria, la sintomatología prefrontal y el estrés percibido. *Rev Neurol*, *54*, 137-50. https://doi.org/10.33588/rn.5403.2011283

Luck, S. J. (2014). An introduction to the event-related potential technique (2nd ed.). The MIT Press.

Luck, S. J., & Gaspelin, N. (2017). How to get statistically significant effects in any ERP experiment (and why you shouldn't). *Psychophysiology*, *54*(1), 146–157. https://doi.org/10.1111/PSYP.12639

Luck, S. J., & Kappenman, E. S. (Eds.). (2011). *The Oxford handbook of event-related potential components*. Oxford university press.

Luck, S. J., Woodman, G. F., & Vogel, E. K. (2000). Event-related potential studies of attention. *Trends in Cognitive Sciences*, *4*(11), 432–440. https://doi.org/10.1016/s1364-6613(00)01545-x

Lundqvist, D., Flykt, A., & Öhman, A. (1998). *The Karolinska directed emotional faces- KDEF, CD ROM from department of clinical neuroscience, psychology section. Karolinska Institutet*. ISBN 91-630-7164-9.

Luo, W., Feng, W., He, W., Wang, N. Y., & Luo, Y. J. (2010). Three stages of facial expression processing: ERP study with rapid serial visual presentation. *NeuroImage*, *49*(2), 1857–1867. https://doi.org/10.1016/j.neuroimage.2009.09.018

Markova, H., Andel, R., Stepankova, H., Kopecek, M., Nikolai, T., Hort, J., Thomas-Antérion, C., & Vyhnalek, M. (2017). Subjective Cognitive Complaints in Cognitively Healthy Older Adults and Their Relationship to Cognitive Performance and Depressive Symptoms. *Journal of Alzheimer's Disease*, *59*(3), 871–881. https://doi.org/10.3233/jad-160970

Mather, M., & Carstensen, L. L. (2005). Aging and motivated cognition: The positivity effect in attention and memory. *Trends in Cognitive Sciences*, 9(10), 496– 502. https://doi.org/10.1016/j.tics.2005.08.005

Mathersul, D., Palmer, D. M., Gur, R. C., Gur, R. E., Cooper, N., Gordon, E., & Williams, L. M. (2009). Explicit identification and implicit recognition of facial emotions: II. Core domains and relationships with general cognition. *Journal of Clinical and Experimental Neuropsychology*, *31*(3), 278–291. https://doi.org/10.1080/13803390802043619

McCade, D., Savage, G., & Naismith, S. L. (2011). Review of Emotion Recognition in Mild Cognitive Impairment. *Dementia and Geriatric Cognitive Disorders*, *32*(4), 257–266. https://doi.org/10.1159/000335009

Mendes, T., Ginó, S., Ribeiro, F., Guerreiro, M., de Sousa, G., Ritchie, K., & de Mendonça, A. (2008). Memory complaints in healthy young and elderly adults: Reliability of memory reporting. *Aging and Mental Health*, *12*(2), 177–182. https://doi.org/10.1080/13607860701797281

Metternich, B., Schmidtke, K., & Hüll, M. (2009). How are memory complaints in functional memory disorder related to measures of affect, metamemory and cognition? *Journal of Psychosomatic Research*, *66*(5), 435–444. https://doi.org/10.1016/J.JPSYCHORES.2008.07.005

Mewton, L., Sachdev, P., Anderson, T., Sunderland, M., & Andrews, G. (2014). Demographic, clinical, and lifestyle correlates of subjective memory complaints in the Australian population. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry*, *22*(11), 1222–1232. https://doi.org/10.1016/J.JAGP.2013.04.004

Meyer, O. L., Leggett, A., Liu, S., & Nguyen, N. H. (2017). Prevalence and correlates of subjective memory complaints in Vietnamese adults. *International Psychogeriatrics*, *30*(7), 1039–1048. https://doi.org/10.1017/s104161021700254x

Michels, L., Muthuraman, M., Anwar, A. R., Kollias, S., Leh, S. E., Riese, F., Unschuld, P. G., Siniatchkin, M., Gietl, A. F., & Hock, C. (2017). Changes of Functional and Directed Resting-State Connectivity Are Associated with Neuronal Oscillations, ApoE Genotype and Amyloid Deposition in Mild Cognitive Impairment. *Frontiers in Aging Neuroscience*, *9*(0),304. https://doi.org/10.3389/fnagi.2017.00304

Mitchell, A. J., Beaumont, H., Ferguson, D., Yadegarfar, M., & Stubbs, B. (2014). Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: meta-analysis. *Acta Psychiatrica Scandinavica*, *130*(6), 439–451. https://doi.org/10.1111/acps.12336

Molina-Rodríguez, S., Pellicer-Porcar, O., & Mirete-Fructuoso, M. (2018). Perceived stress and subjective memory complaints in young adults: The mediating role of the executive functions. *Revista de Neurologia*, *67*(3), 84–90. https://doi.org/10.33588/rn.6703.2017466

Molina-Rodríguez, S., Pellicer-Porcar, O., Mirete-Fructuoso, M., & Martínez-Amorós, E. (2016). Subjective memory complaints, perceived stress and coping strategies in young adults. *Revista de Neurologia*, *62*(8), 344–350. https://doi.org/10.33588/rn.6208.2015496

Montagne, B., Kessels, R. P. C., Frigerio, E., Haan, E. H. F., & Perrett, D. I. (2005). Sex differences in the perception of affective facial expressions: Do men really lack emotional sensitivity? *Cognitive Processing*, *6*(2), 136–141. https://doi.org/10.1007/s10339-005-0050-6

Montejo Carrasco, P., Montenegro Peña, M., Prada Crespo, D., García Mulero, E., García Marín, A., & Pedrero Pérez, E. J. (2019). Quejas de memoria: salud mental, enfermedades, dolor y soledad. Estudio poblacional en la ciudad de Madrid. *Revista De Neurología*, *69*(12), 481. https://doi.org/10.33588/rn.6912.2019252

Montejo, P., Montenegro, M., Fernández, M. A., & Maestú, F. (2011). Subjective memory complaints in the elderly: Prevalence and influence of temporal orientation, depression and quality of life in a population-based study in the city of Madrid. *Aging & Mental Health*, *15*(1), 85–96. https://doi.org/10.1080/13607863.2010.501062

Montenegro, M., Montejo, P., Claver-Martín, M. D., Reinoso, A. I., de Andrés-Montes, M. E., Garcia-Marin, A., Llanero-Luque, M., & Huertas, E. (2013). Relationship between memory complaints and memory performance, mood and sociodemographic variables in young adults. *Revista de neurologia*, *57*(9), 396-404. https://doi.org/10.33588/rn.5709.2013047

Moran, T. P., Jendrusina, A. A., & Moser, J. S. (2013). The psychometric properties of the late positive potential during emotion processing and regulation. *Brain Research*, *1516*, 66–75. https://doi.org/10.1016/J.BRAINRES.2013.04.018

Moretti, D., Miniussi, C., Frisoni, G., Geroldi, C., Zanetti, O., Binetti, G., & Rossini, P. (2007). Hippocampal atrophy and EEG markers in subjects with mild cognitive impairment. *Clinical Neurophysiology*, *118*(12), 2716–2729. https://doi.org/10.1016/j.clinph.2007.09.059

Morgan, H. M., Klein, C., Boehm, S. G., Shapiro, K. L., & Linden, D. E. (2008). Working memory load for faces modulates P300, N170, and N250r. *Journal of Cognitive Neuroscience*, 20(6), 989– 1002. https://doi.org/10.1162/jocn.2008.20072

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, *9*(1), 97–113. https://doi.org/10.1016/0028-3932(71)90067-4

Olofsson, J. K., Nordin, S., Sequeira, H., & Polich, J. (2008). Affective picture processing: An integrative review of ERP findings. *Biological Psychology*, *77*(3), 247–265. https://doi.org/10.1016/j.biopsycho.2007.11.006

Pan, D. N., Wang, Y., Lei, Z., Wang, Y., & Li, X. (2019). The altered early components and the decisive later process underlying attention bias modification in social anxiety: evidence from event-related potentials. *Social Cognitive and Affective Neuroscience*, *14*(12), 1307. https://doi.org/10.1093/SCAN/NSZ098

Park, S., Lee, J. H., Lee, J., Cho, Y., Park, H. G., Yoo, Y., Youn, J. H., Ryu, S. H., Hwang, J. Y., Kim, J., & Lee, J. Y. (2019). Interactions between subjective memory complaint and objective cognitive deficit on memory performances. *BMC Geriatrics*, *19*(1). https://doi.org/10.1186/s12877-019-1322-9

Pavarini, S. C. I., Brigola, A. G., Luchesi, B. M., Souza, É. N., Rossetti, E. S., Fraga, F. J., Guarisco, L. P. C., Terassi, M., Oliveira, N. A., Hortense, P., Pedroso, R. V., & Ottaviani, A. C. (2018). On the use of the P300 as a tool for cognitive processing assessment in healthy aging: A review. *Dementia & Neuropsychologia*, 12(1), 1– 11. https://doi.org/10.1590/1980-57642018dn12-010001

Pellicer-Porcar, O., Mirete-Fructuoso, M., Molina-Rodríguez, S., & Soto-Amaya, J. (2014). Quejas subjetivas de memoria en adultos jóvenes: influencia del estado emocional. *Revista de Neurologia*, *59*(12), 543–550. https://doi.org/10.33588/rn.5912.2014457

Peña-Casanova, J. (1991). Programa integrado de exploración neuropsicológica - test barcelona: bases teóricas, objetivos y contenidos. *Revista De Logopedia, Foniatría y Audiología*, *11*(2), 66–79. https://doi.org/10.1016/s0214-4603(91)75505-8

Perez, V., Garrido-Chaves, R., Zapater-Fajarí, M., Pulopulos, M. M., Barbosa, F., Hidalgo, V., & Salvador, A. (2021). Deficits in facial emotional valence processing in older people with subjective memory complaints: Behavioral and electrophysiological evidence. *Psychophysiology*, e13989. https://doi.org/10.1111/psyp.13989

Pessoa, L. (2009). How do emotion and motivation direct executive control? *Trends in Cognitive Sciences*, *13*(4), 160–166. https://doi.org/10.1016/j.tics.2009.01.006

Peter, J., Scheef, L., Abdulkadir, A., Boecker, H., Heneka, M., Wagner, M., Koppara, A., Klöppel, S., & Jessen, F. (2014). Gray matter atrophy pattern in elderly with subjective memory impairment. *Alzheimer's & Dementia*, 10(1), 99– 108. https://doi.org/10.1016/j.jalz.2013.05.1764

Petersen, S. E., & Posner, M. I. (2012). The Attention System of the Human Brain: 20 Years After. *Annual Review of Neuroscience*, *35*(1), 73–89. https://doi.org/10.1146/annurev-neuro-062111-150525

Pettigrew, C., & Soldan, A. (2019). Defining Cognitive Reserve and Implications for Cognitive Aging. *Current Neurology and Neuroscience Reports*, *19*(1), 1. https://doi.org/10.1007/S11910-019-0917-Z

Phillips, L. H., Channon, S., Tunstall, M., Hedenstrom, A., & Lyons, K. (2008). The role of working memory in decoding emotions. *Emotion*, *8*(2), 184–191. https://doi.org/10.1037/1528-3542.8.2.184

Phillips, M. L., Drevets, W. C., Rauch, S. L., & Lane, R. (2003). Neurobiology of emotion perception I: the neural basis of normal emotion perception. *Biological Psychiatry*, *54*(5), 504–514. https://doi.org/10.1016/s0006-3223(03)00168-9

Pietschnig, J., Aigner-Wöber, R., Reischenböck, N., Kryspin-Exner, I., Moser, D., Klug, S., Auff, E., Dal-Bianco, P., Pusswald, G., & Lehrner, J. (2015). Facial emotion recognition in patients with subjective cognitive decline and mild cognitive impairment. *International Psychogeriatrics*, *28*(3), 477–485. https://doi.org/10.1017/S1041610215001520

Pijnenburg, Y. A. L., Strijers, R. L. M., Made, Y. vd, van der Flier, W. M., Scheltens, P., & Stam, C. J. (2008). Investigation of resting-state EEG functional connectivity in frontotemporal lobar degeneration. *Clinical Neurophysiology*, *119*(8), 1732–1738. https://doi.org/10.1016/J.CLINPH.2008.02.024

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*, *118*(10), 2128–2148. https://doi.org/10.1016/j.clinph.2007.04.019

Polich, J., & Kok, A. (1995). Cognitive and biological determinants of P300: an integrative review. *Biological Psychology*, *41*(2), 103–146. https://doi.org/10.1016/0301-0511(95)05130-9

Poncet, F., Baudouin, J. Y., Dzhelyova, M. P., Rossion, B., & Leleu, A. (2019). Rapid and automatic discrimination between facial expressions in the human brain. *Neuropsychologia*, *129*, 47–55. https://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2019.03.006

Prichep, L., John, E., Ferris, S., Reisberg, B., Almas, M., Alper, K., & Cancro, R. (1994). Quantitative EEG correlates of cognitive deterioration in the elderly. *Neurobiology of Aging*, *15*(1), 85–90. https://doi.org/10.1016/0197-4580(94)90147-3

Proudfit, G. H., Dunning, J. P., Foti, D., & Weinberg, A. (2014). Temporal dynamics of emotion regulation. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 43–57). The Guilford Press.

Proverbio, A. M. (2017). Sex differences in social cognition: The case of face processing. *Journal of Neuroscience Research*, *95*(1–2), 222–234. https://doi.org/10.1002/JNR.23817

Qiu, R., Wang, H., & Fu, S. (2017). N170 Reveals the Categorical Perception Effect of Emotional Valence. *Frontiers in Psychology*, *8*. https://doi.org/10.3389/fpsyg.2017.02056

Rami, L., Valls-Pedret, C., Bartrés-Faz, D., Caprile, C., Solé-Padullés, C., Castellví, M., Olives, J., Bosch, B., & Molinuevo, J. L. (2011). Cognitive reserve questionnaire. Scores obtained in a healthy elderly population and in one with Alzheimer's disease. *Revista de Neurologia*, *52*(4), 195–201. https://doi.org/10.33588/rn.5204.2010478

Rathee, S., Bhatia, D., Punia, V., & Singh, R. (2020). Peak Alpha Frequency in Relation to Cognitive Performance. *Journal of Neurosciences in Rural Practice*, *11*(3), 416. https://doi.org/10.1055/S-0040-1712585

Reid, L. M., & MacLullich, A. M. (2006). Subjective Memory Complaints and Cognitive Impairment in Older People. *Dementia and Geriatric Cognitive Disorders*, *22*(5), 471–485. https://doi.org/10.1159/000096295

Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. Am J Psychiatry 1982; 139: 1136–39.

Reitan, R. M. (1992). *Trail making test: Manual for administration and scoring*. Reitan Neuropsychology Laboratory, Length.

Roh, J. H., Park, M. H., Ko, D., Park, K. W., Lee, D. H., Han, C., Jo, S. A., Yang, K. S., & Jung, K. Y. (2011). Region and frequency specific changes of spectral power in Alzheimer's disease and mild cognitive impairment. *Clinical Neurophysiology*, *122*(11), 2169–2176. https://doi.org/10.1016/j.clinph.2011.03.023

Rönnlund, M., Sundström, A., Adolfsson, R., & Nilsson, L. G. (2015). Subjective memory impairment in older adults predicts future dementia independent of baseline memory performance: Evidence from the Betula prospective cohort study. *Alzheimer's & Dementia*, 11(11), 1385– 1392. https://doi.org/10.1016/j.jalz.2014.11.006

Rossini, P. M., & Forno, G. D. (2004). Integrated technology for evaluation of brain function and neural plasticity. *Physical Medicine and Rehabilitation Clinics of North America*, *15*(1), 263–306. https://doi.org/10.1016/s1047-9651(03)00124-4

Rossini, P. M., Rossi, S., Babiloni, C., & Polich, J. (2007). Clinical neurophysiology of aging brain: From normal aging to neurodegeneration. *Progress in Neurobiology*, *83*(6), 375–400. https://doi.org/10.1016/j.pneurobio.2007.07.010

Rossini, P., Percio, C. D., Pasqualetti, P., Cassetta, E., Binetti, G., Forno, G. D., Ferreri, F., Frisoni, G., Chiovenda, P., Miniussi, C., Parisi, L., Tombini, M., Vecchio, F., & Babiloni, C. (2006). *Conversion from mild cognitive impairment to Alzheimer's disease is predicted by sources and coherence of brain electroencephalography rhythms*. *143*(3), 793–803. https://doi.org/10.1016/j.neuroscience.2006.08.049

Rossion, B. (2014). Understanding face perception by means of human electrophysiology. *Trends in Cognitive Sciences*, *18*(6), 310–318. https://doi.org/10.1016/j.tics.2014.02.013

Rossion, B., & Jacques, C. (2008). Does physical interstimulus variance account for early electrophysiological face sensitive responses in the human brain? Ten lessons on the N170. *NeuroImage*, *39*(4), 1959–1979. https://doi.org/10.1016/j.neuroimage.2007.10.011

Rowell, S. F., Green, J. S., Teachman, B. A., & Salthouse, T. A. (2015). Age does not matter: Memory complaints are related to negative affect throughout adulthood. *Aging & Mental Health*, *20*(12), 1255–1263. https://doi.org/10.1080/13607863.2015.1078284

Ruffman, T., Henry, J. D., Livingstone, V., & Phillips, L. H. (2008). A meta-analytic review of emotion recognition and aging: implications for neuropsychological models of aging. *Neuroscience and Biobehavioral Reviews*, *32*(4), 863–881. https://doi.org/10.1016/J.NEUBIOREV.2008.01.001

Ruiz-Gómez, S. J., Gómez, C., Poza, J., Gutiérrez-Tobal, G. C., Tola-Arribas, M. A., Cano, M., & Hornero, R. (2018). Automated Multiclass Classification of Spontaneous EEG Activity in Alzheimer's Disease and Mild Cognitive Impairment. *Entropy 2018, Vol. 20, Page 35*, *20*(1), 35. https://doi.org/10.3390/E20010035

Ruiz-Sanchez de Leon, J. M., Llanero-Luque, M., Lozoya-Delgado, P., Fernandez-Blazquez, M. A., & Pedrero-Perez, E. J. (2010). Neuropsychological study of young adults with subjective memory complaints: involvement of the executive functions and other associated frontal symptoms. *Revista de neurologia*, *51*(11), 650-660. https://doi.org/10.33588/rn.5111.2010270

Sadeh, B., Podlipsky, I., Zhdanov, A., & Yovel, G. (2010). Event-related potential and functional MRI measures of face-selectivity are highly correlated: A simultaneous ERP-fMRI investigation. *Human Brain Mapping*, *31*(10), 1490–1501. https://doi.org/10.1002/hbm.20952

Sagiv, N., & Bentin, S. (2001). Structural Encoding of Human and Schematic Faces: Holistic and Part-Based Processes. *Journal of Cognitive Neuroscience*, *13*(7), 937–951. https://doi.org/10.1162/089892901753165854

Sander, D., Grandjean, D., Pourtois, G., Schwartz, S., Seghier, M. L., Scherer, K. R., & Vuilleumier, P. (2005). Emotion and attention interactions in social cognition: brain regions involved in processing anger prosody. *NeuroImage*, *28*(4), 848–858. https://doi.org/10.1016/J.NEUROIMAGE.2005.06.023

Sarabia-Cobo, C. M., García-Rodríguez, B., Navas, M. J., & Ellgring, H. (2015). Emotional processing in patients with mild cognitive impairment: The influence of the valence and intensity of emotional stimuli. *Journal of the Neurological Sciences*, *357*(1), 222–228. https://doi.org/10.1016/j.jns.2015.07.034

Sarter, M., & Bruno, J. P. (1998). Cortical Acetylcholine, Reality Distortion, Schizophrenia, and Lewy Body Dementia: Too Much or Too Little Cortical Acetylcholine? *Brain and Cognition*, *38*(3), 297–316. https://doi.org/10.1006/brcg.1998.1035

Sato, W., Kochiyama, T., Uono, S., Matsuda, K., Usui, K., Usui, N., Inoue, Y., & Toichi, M. (2017). Bidirectional electric communication between the inferior occipital gyrus and the amygdala during face processing. *Human Brain Mapping*, *38*(9), 4511. https://doi.org/10.1002/HBM.23678

Sauseng, P., Klimesch, W., Gruber, W., Doppelmayr, M., Stadler, W., & Schabus, M. (2002). The interplay between theta and alpha oscillations in the human electroencephalogram reflects the transfer of information between memory systems. *Neuroscience Letters*, *324*(2), 121–124. https://doi.org/10.1016/s0304-3940(02)00225-2

Scally, B., Burke, M. R., Bunce, D., & Delvenne, J. F. (2018). Resting-state EEG power and connectivity are associated with alpha peak frequency slowing in healthy aging. *Neurobiology of Aging*, *71*, 149–155. https://doi.org/10.1016/J.NEUROBIOLAGING.2018.07.004

Schefter, M., Knorr, S., Kathmann, N., & Werheid, K. (2012). Age differences on ERP old/new effects for emotional and neutral faces. *International Journal of Psychophysiology*, *85*(2), 257–269. https://doi.org/10.1016/j.ijpsycho.2011.11.011

Schindler, S., & Bublatzky, F. (2020). Attention and emotion: An integrative review of emotional face processing as a function of attention. *Cortex*, *130*(0), 362–386. https://doi.org/10.1016/j.cortex.2020.06.010

Schmand, B., Jonker, C., Hooijer, C., & Lindeboom, J. (1996). Subjective memory complaints may announce dementia. *Neurology*, *46*(1), 121–125. https://doi.org/10.1212/WNL.46.1.121

Schumacher, J., Thomas, A. J., Peraza, L. R., Firbank, M., Cromarty, R., Hamilton, C. A., Donaghy, P. C., O'Brien, J. T., & Taylor, J. P. (2020). EEG alpha reactivity and cholinergic system integrity in Lewy body dementia and Alzheimer's disease. *Alzheimer's Research & Therapy*, *12*(1). https://doi.org/10.1186/s13195-020-00613-6

Schupp, H. T., Cuthbert, B. N., Bradley, M. M., Cacioppo, J. T., Ito, T., & Lang, P. J. (2000). Affective picture processing: The late positive potential is modulated by motivational relevance. *Psychophysiology*, *37*(2), 257–261. https://doi.org/10.1111/1469-8986.3720257

Schupp, H. T., Flaisch, T., Stockburger, J., & Junghöfer, M. (2006). Emotion and attention: event-related brain potential studies. *Progress in Brain Research*, *0*(0), 31–51. https://doi.org/10.1016/s0079-6123(06)56002-9

Schütz, H., Caspers, S., Moebus, S., & Lux, S. (2020). Prevalence and psychosocial correlates of subjectively perceived decline in five cognitive domains: Results from a population-based cohort study in Germany. *International Journal of Geriatric Psychiatry*, *35*(10), 1219–1227. https://doi.org/10.1002/gps.5359

Schweizer, S., Kievit, R. A., Emery, T., & and, R. N. H. (2017). Symptoms of depression in a large healthy population cohort are related to subjective memory complaints and memory performance in negative contexts. *Psychological Medicine*, *48*(1), 104–114. https://doi.org/10.1017/s0033291717001519

Self, D. (2009). Audio power amplifier design handbook (5th ed., p. 541). Burlington, MA: Elsevier.

Sleimen-Malkoun, R., Perdikis, D., Müller, V., Blanc, J. L., Huys, R., Temprado, J. J., & Jirsa, V. K. (2015). Brain Dynamics of Aging: Multiscale Variability of EEG Signals at Rest and during an Auditory Oddball Task. *Eneuro*, *2*(3), ENEURO.0067–0014.2015. https://doi.org/10.1523/eneuro.0067-14.2015

Smart, C. M., Segalowitz, S. J., Mulligan, B. P., & MacDonald, S. W. (2014). Attention capacity and self-report of subjective cognitive decline: A P3 ERP study. *Biological Psychology*, 103, 144– 151. https://doi.org/10.1016/j.biopsycho.2014.08.016

Sohrabi, H. R., Weinborn, M., Laske, C., Bates, K. A., Christensen, D., Taddei, K., Rainey-Smith, S. R., Brown, B. M., Gardener, S. L., Laws, S. M., Martins, G., Burnham, S. C., Bucks, R. S., Reisberg, B., Lautenschlager, N. T., Foster, J., & Martins, R. N. (2018). Subjective memory complaints predict baseline but not future cognitive function over three years: results from the Western Australia Memory Study. *International Psychogeriatrics*, *31*(4), 513–525. https://doi.org/10.1017/s1041610218001072

Soto, V., Tyson-Carr, J., Kokmotou, K., Roberts, H., Cook, S., Fallon, N., Giesbrecht, T., & Stancak, A. (2018). Brain responses to emotional faces in natural settings: A wireless mobile EEG recording study. *Frontiers in Psychology*, *9*(OCT), 2003. https://doi.org/10.3389/FPSYG.2018.02003/BIBTEX

Spoletini, I., Marra, C., Iulio, F. di, Gianni, W., Sancesario, G., Giubilei, F., Trequattrini, A., Bria, P., Caltagirone, C., & Spalletta, G. (2008). Facial emotion recognition deficit in amnestic mild cognitive impairment and Alzheimer disease. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry*, *16*(5), 389–398. https://doi.org/10.1097/JGP.0B013E318165DBCE

Stenfors, C. U. D., Marklund, P., Hanson, L. L. M., Theorell, T., & Nilsson, L. G. (2013). Subjective Cognitive Complaints and the Role of Executive Cognitive Functioning in the Working Population: A Case-Control Study. *PLoS ONE*, *8*(12), e83351. https://doi.org/10.1371/journal.pone.0083351

Stern, Y. (2009). Cognitive reserve. *Neuropsychologia*, *47*(10), 2015–2028. https://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2009.03.004

Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *The Lancet. Neurology*, *11*(11), 1006–1012. https://doi.org/10.1016/S1474-4422(12)70191-6

Stocker, R. P. J., Khan, H., Henry, L., & Germain, A. (2017). Effects of Sleep Loss on Subjective Complaints and Objective Neurocognitive Performance as Measured by the Immediate Post-Concussion Assessment and Cognitive Testing. *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists*, *32*(3), 349–368. https://doi.org/10.1093/ARCLIN/ACX003

Striepens, N., Scheef, L., Wind, A., Popp, J., Spottke, A., Cooper-Mahkorn, D., Suliman, H., Wagner, M., Schild, H. H., & Jessen, F. (2010). Volume Loss of the Medial Temporal Lobe Structures in Subjective Memory Impairment. *Dementia and Geriatric Cognitive Disorders*, *29*(1), 75–81. https://doi.org/10.1159/000264630

Sun, L., Ren, J., & He, W. (2017). Neural correlates of facial expression processing during a detection task: An ERP study. *PLOS ONE*, *12*(3), e0174016. https://doi.org/10.1371/JOURNAL.PONE.0174016

Sun, T., Li, L., Xu, Y., Zheng, L., Zhang, W., Zhou, F. A., & Guo, X. (2017). Electrophysiological evidence for women superiority on unfamiliar face processing. *Neuroscience Research*, *115*, 44–53. https://doi.org/10.1016/j.neures.2016.10.002

Sunderland, A., Harris, J. E., & Gleave, J. (1984). Memory failures in everyday life following severe head injury. *Journal of Clinical Neuropsychology*, *6*(2), 127–142. https://doi.org/10.1080/01688638408401204

Sutton S. P300 – thirteen years later. In: Begleiter H, editor. Evoked brain potentials and behavior. New York: Plenum Press; 1979. p. 107–25

Teng, E., Lu, P. H., & Cummings, J. L. (2007). Deficits in Facial Emotion Processing in Mild Cognitive Impairment. *Dementia and Geriatric Cognitive Disorders*, *23*(4), 271–279. https://doi.org/10.1159/000100829

Usakli, A. B. (2010). Improvement of EEG Signal Acquisition: An Electrical Aspect for State of the Art of Front End. *Computational Intelligence and Neuroscience*, *2010*(0), 1–7. https://doi.org/10.1155/2010/630649

Van Flier, W., Buchem, M., Weverling-Rijnsburger, A., Mutsaers, E., Bollen, E., Admiraal-Behloul, F., Westendorp, R., & Middelkoop, H. (2004). Memory complaints in patients with normal cognition are associated with smaller hippocampal volumes. *Journal of Neurology*, *251*(6). https://doi.org/10.1007/s00415-004-0390-7

Van Strien, J. W. V., Sonneville, L. M. D., & Franken, I. H. (2010). The late positive potential and explicit versus implicit processing of facial valence. *NeuroReport*, *21*(9), 656–661. https://doi.org/10.1097/WNR.0b013e32833ab89e

Vaqué-Alcázar, L., Sala-Llonch, R., Valls-Pedret, C., Vidal-Piñeiro, D., Fernández-Cabello, S., Bargalló, N., Ros, E., & Bartrés-Faz, D. (2017). Differential age-related gray and white matter impact mediates educational influence on elders' cognition. *Brain Imaging and Behavior*, *11*(2), 318–332. https://doi.org/10.1007/S11682-016-9584-8/TABLES/3

Varjassyová, A., Hořínek, D., Andel, R., Amlerova, J., Laczó, J., Sheardová, K., Magerová, H., Holmerová, I., Vyhnálek, M., Bradáč, O., & al. (2012). Recognition of Facial Emotional Expression in Amnestic Mild Cognitive Impairment. *Journal of Alzheimer's Disease*, *33*(1), 273–280. https://doi.org/10.3233/JAD-2012-120148

Vaskivuo, L., Hokkanen, L., Hänninen, T., Antikainen, R., Bäckman, L., Laatikainen, T., Paajanen, T., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto, J., Soininen, H., Kivipelto, M., & Ngandu, T. (2018). Associations between Prospective and Retrospective Subjective Memory Complaints and Neuropsychological Performance in Older Adults: The Finger Study. *Journal of the International Neuropsychological Society*, *24*(10), 1099–1109. https://doi.org/10.1017/S135561771800053X

Verhallen, R. J., Bosten, J. M., Goodbourn, P. T., Lawrance-Owen, A. J., Bargary, G., & Mollon, J. (2017). General and specific factors in the processing of faces. *Vision Research*, *141*(0), 217–227. https://doi.org/10.1016/j.visres.2016.12.014

Vlachos, G. S., Cosentino, S., Kosmidis, M. H., Anastasiou, C. A., Yannakoulia, M., Dardiotis, E., Hadjigeorgiou, G., Sakka, P., Ntanasi, E., & Scarmeas, N. (2019). Prevalence and determinants of subjective cognitive decline in a representative Greek elderly population. *International Journal of Geriatric Psychiatry*, *34*(6), 846–854. https://doi.org/10.1002/gps.5073

Vysata, O., Kukal, J., Prochazka, A., Pazdera, L., & Valis, M. (2012). Age-Related Changes in the Energy and Spectral Composition of EEG. *Neurophysiology*, *44*(1), 63–67. https://doi.org/10.1007/s11062-012-9268-y

Wada, Y., Takizawa, Y., Zheng-Yan, J., & Yamaguchi, N. (1994). Gender Differences in Quantitative EEG at Rest and during Photic Stimulation in Normal Young Adults. *Clinical Electroencephalography*, *25*(2), 81–85. https://doi.org/10.1177/155005949402500209

Wan, L., Huang, H., Schwab, N., Tanner, J., Rajan, A., Lam, N. B., Zaborszky, L., Li, C. S. R., Price, C. C., & Ding, M. (2018). From eyes-closed to eyes-open: Role of cholinergic projections in EC-to-EO alpha reactivity revealed by combining EEG and MRI. *Human Brain Mapping*, *40*(2), 566–577. https://doi.org/10.1002/hbm.24395

Wang, H., McIntosh, A. R., Kovacevic, N., Karachalios, M., & Protzner, A. B. (2016). Age-related Multiscale Changes in Brain Signal Variability in Pre-task versus Post-task Resting-state EEG. *Journal of Cognitive Neuroscience*, *28*(7), 971–984. https://doi.org/10.1162/jocn_a_00947

Wang, X., Yang, L., Zhao, X., Wang, L., Yu, L., & Song, M. (2015). Emotional face recognition deficit in amnestic patients with mild cognitive impairment: behavioral and electrophysiological evidence. *Neuropsychiatric Disease and Treatment*, 1973. https://doi.org/10.2147/ndt.s85169

Ward, L. M. (2003). Synchronous neural oscillations and cognitive processes. *Trends in Cognitive Sciences*, *7*(12), 553–559. https://doi.org/10.1016/j.tics.2003.10.012

Wechsler, D. (1997). *WMS-III: Wechsler memory scale administration and scoring manual*. Psychological Corporation

Whitham, E. M., Pope, K. J., Fitzgibbon, S. P., Lewis, T., Clark, C. R., Loveless, S., Broberg, M., Wallace, A., DeLosAngeles, D., Lillie, P., Hardy, A., Fronsko, R., Pulbrook, A., & Willoughby, J. O. (2007). Scalp electrical recording during paralysis: Quantitative evidence that EEG frequencies above 20Hz are contaminated by EMG. *Clinical Neurophysiology*, *118*(8), 1877–1888. https://doi.org/10.1016/j.clinph.2007.04.027

WHO (2018). *Ageing and health*. Retrieved from https://www.who.int/news-room/factsheets/detail/ageing-and-health

Yang, L., Zhao, X., Wang, L., Yu, L., Song, M., & Wang, X. (2015). Emotional face recognition deficit in amnestic patients with mild cognitive impairment: behavioral and electrophysiological evidence. Neuropsychiatric disease and treatment, 11, 1973. https://doi.org/10.2147/NDT.S85169

Yoon, S., Shim, M., Kim, H. S., & Lee, S. H. (2016). Enhanced Early Posterior Negativity to Fearful Faces in Patients with Anxiety Disorder. *Brain Topography*, *29*(2), 262–272. https://doi.org/10.1007/S10548-015-0456-0

Zhang, L., Qin, S., Yao, Z., Zhang, K., & Wu, J. (2016). Long-term academic stress enhances early processing of facial expressions. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology*, *109*, 138–146. https://doi.org/10.1016/J.IJPSYCHO.2016.08.010

Zhao, J., Meng, Q., An, L., & Wang, Y. (2019). An event-related potential comparison of facial expression processing between cartoon and real faces. *PLOS ONE*, *14*(1), e0198868. https://doi.org/10.1371/journal.pone.0198868

Zhao, Q., Tang, Y., Chen, S., Lyu, Y., Curtin, A., Wang, J., Sun, J., & Tong, S. (2015). Early perceptual anomaly of negative facial expression in depression: An event-related potential study. *Neurophysiologie Clinique = Clinical Neurophysiology*, *45*(6), 435–443. https://doi.org/10.1016/J.NEUCLI.2015.09.011

Zlatar, Z. Z., Muniz, M., Galasko, D., & Salmon, D. P. (2018). Subjective Cognitive Decline Correlates With Depression Symptoms and Not With Concurrent Objective Cognition in a Clinic-Based Sample of Older Adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *73*(7), 1198. https://doi.org/10.1093/GERONB/GBW207

FUNDING SOURCE

The research reported in this study was supported by the Spanish Education and Science Ministry with grant no. PSI2016-78763-P and PSI2017-90806-REDT.