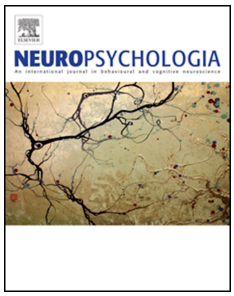

Active bilingualism delays the onset of mild cognitive impairment

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Active bilingualism delays the onset of mild cognitive impairment

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Abstract

Lifelong bilingualism may contribute to cognitive reserve (CR) in neurodegenerative diseases as shown by a delay of the age at symptom onset in bilinguals with Alzheimer's disease (AD) and Mild Cognitive Impairment (MCI). However, some studies have failed to show this bilingual advantage, suggesting that it might depend on the type and degree of bilingualism. In the present study, we tested the hypothesis that active bilingualism, defined as the continuous use of the two languages as opposed to second language exposition only, may protect against cognitive decline. Moreover, we investigated whether bilingualism as a CR factor may be explained by an advantage within the executive control (EC) system.

To do so, we collected clinical measures (age at onset of cognitive symptoms, age at the first medical visit for cognitive impairments, and age at diagnosis) in patients with MCI and patients with AD with different degrees of language experience and usage of Catalan and Spanish. Additionally, all participants were tested on four EC tasks and one long-term memory recognition task.

First, results from multiple regression analyses showed that active bilingualism was a significant predictor of delay in the age at onset for all the clinical measures in MCI, but not AD patients. Second, the effect of active bilingualism was independent of occupation, educational level and job attainment across the individuals' lifespan. Finally, although we did not find an effect of active bilingualism across all EC tasks, we did find an effect for conflict resolution.

These results are discussed in the context of CR hypotheses, suggesting that compensatory mechanisms may play a role in protecting against cognitive decline.

Keywords: Alzheimer's disease, bilingualism, cognitive reserve, cognitive resilience, mild cognitive impairment, executive control

1. Introduction

The prevalence of dementia in countries with bilingual or multilingual speakers is half that of countries where populations use only one language to communicate (Klein, Christie, & Parkvall, 2016). While other social and environmental factors might also contribute to such a stark difference in prevalence, this worldwide study seems to support the idea that lifelong usage of two languages may be an important factor in enhancing cognitive reserve. In fact, about 60% of studies on this phenomenon have shown that bilingualism may delay the onset of dementia, or impart some advantage in memory and/or executive functioning (Calvo, García, Manoiloff, & Ibáñez, 2016). In spite of this, whether or not bilingualism confers any benefit in age-related disorders remains a hotly debated topic. On the one hand, the linguistic profile of a bilingual, i.e language proficiency (Bialystok & Feng, 2009; Xie, 2018) and usage (de Bruin, 2020), as well as other cognitive reserve factors, i.e.- social activity (Evans et al., 2018; Scarmeas & Stern, 2003) and occupation (Darwish, Farran, Assaad, & Chaaya, 2018), might act to highlight or, conversely, mask such a bilingual advantage. On the other hand, the incomplete understanding of what drives the effect (if any) (Bak, 2016) makes it more difficult to define the outcome measures and thus increases the probability of false conclusions.

In the present study, we focused on these two aspects of bilingualism (i.e.- language proficiency and usage) as cognitive reserve factors in Mild Cognitive Impairment (MCI) and Alzheimer disease (AD). First, we approached the issue of defining bilingualism by using a continuum from passive to active bilingualism, instead of simply classifying participants as monolinguals or bilinguals (for a discussion see Bak, 2016). This methodological approach allows researchers to test participants who have had diverse linguistic experiences—with variation in their second language (L2) usage, years of L2 exposure, and age of L2 acquisition— but who may have been living in the same geographic location; this technique, thus, reduces the potential confounding effects of individual differences in socio-environmental factors.

Second, to better understand the origin of the bilingual advantage, we tested participants on several cognition tasks. We focused more on the executive control (EC) system as its efficiency in

bilinguals has been proposed to be the origin of said advantage (Bialystok, 2011). To this end, we used a set of EC tasks that covered shifting, updating abilities and inhibitory control. We also explored episodic memory due to its pertinence as one of the cognitive domains typically altered by the onset of MCI and AD. Indeed, one might speculate that a greater efficacy of memory functions in bilingual patients may be responsible for the delay in onset of symptoms, as proposed in some studies (e.g. Bak, Nissan, Allerhand, & Deary, 2014; Perani et al., 2017; Rosselli et al., 2019).

1.1. What linguistic profile variables might modulate the bilingual advantage on cognition?

The existence of a bilingual advantage in non-linguistic processes, especially EC, has been brought into question by many studies (de Bruin, Treccani, & Della Sala, 2015; Lehtonen et al., 2018; Paap & Greenberg, 2013; Paap, Johnson, & Sawi, 2015, 2016) and some researchers have proposed that it may depend on the type of bilingualism that is being considered (van den Noort et al., 2019). One key aspect of experimental design that could lead to discrepancy in the literature is that bilingualism cannot be considered as a categorical variable (Luk & Bialystok, 2013) and research has suggested that adults' language profiles may modulate the effects on non-linguistic control.

For instance, individuals with a higher rate of language switching in everyday life showed reduced switch costs associated with reconfiguring a given task in a task-switching paradigm as compared to speakers with lower rates of language switching and monolinguals (Prior and Gollan, 2011). Similarly, bilinguals who suffer less cross-language interference (less intrusions from the non-target language) score better on EC tasks concerning inhibitory control and divided attention than those bilinguals who make more cross-language intrusion errors and thus demonstrate poorer language control (Festman & Münte, 2012; Festman, Rodriguez-Fornells, & Münte, 2010; Rodriguez-Fornells, Krämer, Lorenzo-Seva, Festman, & Münte, 2012). This finding supports the idea that linguistic and non-linguistic systems share similar control mechanisms; therefore, switching more often between two languages could transfer its effects to non-linguistic switching abilities by reducing

the cost associated with conflict resolution (Verreyt, Woumans, Vandelanotte, Szmalec, & Duyck, 2016; but see also Jylkkä et al., 2017).

Other factors that might shape the bilingual advantage are language usage, language proficiency and age of L2 acquisition (Yow & Li, 2015). Despite bilinguals having been shown to hold an advantage in conflict resolution and task switching, the individual differences in language profiles within a given group of bilinguals could modulate the magnitude of the task-associated costs. For instance, Bak, Vega-Mendoza, and Sorace (2014) found that early bilinguals had a greater reduction in switch costs compared to late bilinguals, whereas Tao et al. (2011) showed that late bilinguals with similar use of the two languages had the greatest advantage in conflict resolution, whereas early bilinguals demonstrated enhanced monitoring processes (see also Singh & Mishra, 2013). Similarly, language usage has been shown to have a modulatory effect on the aging-related EC decline in bilinguals. For example, in bilinguals who were balanced in terms of language usage, the magnitude of interference in a conflict task did not increase (Goral, Campanelli, & Spiro, 2015), suggesting a protective effect of these variables associated to bilingualism.

However, the role of these separate linguistic variables in contributing to cognitive benefits for bilingual patients with neurodegenerative diseases has not been explored yet and is arguably a better way to investigate this issue, rather than subscribing to the monolingual-bilingual dichotomy. Moreover, some of these variables are highly correlated; therefore, it is important to explore their degree of contribution to the cognitive benefits associated with bilingualism. To do this, our study considered a composite score of bilingualism (DiStefano, Zhu, & Mîndrilã, 2009). that was calculated based on the weighted contribution of each variable, allowing us to obtain an individual score indicating the degree of bilingualism.

1.2. Bilingualism and cognitive reserve: what are the underlying mechanisms?

Following the pioneering study by Bialystok and collaborators in Canada (Bialystok, Craik, & Freedman, 2007), more studies have reported that bilingualism or multilingualism is a factor of cognitive reserve, delaying the onset of cognitive symptoms associated with AD or MCI by up to 5

years (Alladi et al., 2013; Anderson, Saleemi, & Bialystok, 2017; Chertkow et al., 2010; Craik, Bialystok, & Freedman, 2010; Ossher, Bialystok, Craik, Murphy, & Troyer, 2013; Woumans et al., 2015; Woumans, Versijpt, Sieben, Santens, & Duyck, 2017; for a review Calvo et al., 2016). However, other studies did not find such a bilingual advantage (Crane et al., 2009, 2010; Perquin et al., 2013; Sanders, Hall, Katz, & Lipton, 2012; Zahodne, Schofield, Farrell, Stern, & Manly, 2014), generating a debate over the reliability of bilingualism as a cognitive reserve mechanism and the role of certain factors in determining its presence, such as immigration status, education, age at onset, language proficiency, and frequency of language usage (Guzman-Velez, 2016).

Nevertheless, the most intriguing question about the relationship between cognitive reserve and bilingualism is what drives this effect; that is, what are the underlying mechanisms that allow lifelong usage of two languages to benefit cognition. At least two mechanisms have been described for cognitive and neural reserve (Barulli & Stern, 2013; Stern, 2012; Stern et al., 2018). One would be that individual differences in tolerating the disease-associated neuropathology are related to differences in the efficiency of those areas affected by the disease. That is, cognitive reserve factors act to enhance neural efficiency and this would subsequently protect the brain network affected by AD neuropathology. A second mechanism would be alternative networks: those circuits not affected by the disease could play a compensatory role in protecting against cognitive symptoms. In the context of bilingualism, it seems that both mechanisms may contribute to cognitive reserve. For instance, Schweizer, Ware, Fischer, Craik, & Bialystok (2012) showed that bilinguals had greater amounts of brain atrophy in the areas associated with AD than monolingual peers, despite cognitive decline of both groups being equal (for similar results see Duncan et al., 2018). This means that bilinguals would have a higher threshold for reaching a diagnosis of dementia, likely because the brain areas affected by the disease are more efficient and may cope better with the structural damage. However, some other studies have shown that there could be a compensatory mechanism mediated by the EC network, as suggested by an increased metabolic connectivity in the fronto-parietal network in bilinguals (Perani et al., 2017). In line with this, bilingual older adults have shown to have better functional efficiency (Gold, Kim, Johnson, Kryscio, & Smith, 2013), higher neural efficiency (Abutalebi et al., 2014; Borsa et al., 2018; Del Maschio et al., 2018; Gold, Johnson, & Powell, 2013),

and better connectivity (Grady, Luk, Craik, & Bialystok, 2015; Luk, Bialystok, Craik, & Grady, 2011) within the EC network while performing EC tasks when compared to their monolingual peers.

However, what has been shown to be less consistent are results indicating a more efficient EC system at the behavioural level in bilinguals, at least in patients with AD and MCI. In Anderson, Saleemi, and Bialystok's (2017) study, only bilingual healthy adults (but not MCI or AD bilinguals) showed better inhibitory control than monolinguals (for similar results in AD patients, see Clare et al., 2016). Conversely, Bialystok, Craik, Binns, Ossher, and Freedman (2014) found that bilinguals with AD or MCI exhibit a smaller Stroop effect than monolingual peers, but the trend of decline at one year for both language groups was the same.

Beyond executive functions, some studies reported that long-term memory was more preserved in bilinguals with AD than monolinguals (Perani et al., 2017), suggesting that bilingualism may also act by increasing the efficiency of one of the cognitive domains most affected by AD, episodic memory (see also Bak, Nissan, Allerhand, & Deary, 2014; Ljungberg, Hansson, Andrés, Josefsson, & Nilsson, 2013). Similarly, it has been proposed that bilingual adults' brains might work like those of people with higher degree of cognitive reserve and less affected by the negative effect of aging (Grant, Dennis, & Li, 2014; Grundy, Anderson, & Bialystok, 2017). Indeed, older adults with higher degrees of cognitive reserve or resilience show patterns of functionality in posterior areas comparable to those of young adults, whereas those with low levels of resilience have more frontally-distributed activity and less efficient memory (e.g. Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008).

Thus, in order to better characterise the origin of bilingualism's capacity to delay the onset of cognitive decline, we tested both EC and episodic memory with experimental tasks. Moreover, as EC is made up of various processes, we tested its different sub-components according to what has been proposed by some theoretical models as the differentiation between executive functions.

1.3. The present study

In our study, we introduced some methodological novelties in order to improve the assessment of underlying factors that may promote bilingualism as a cognitive reserve mechanism. First, we

avoided the dichotomous classification of monolinguals versus bilinguals and instead used a number of variables related to the experience of speaking two languages. This allows bilingualism to be treated as a continuum and lets us explore which variables are crucial in making bilingualism a contributing factor to cognitive reserve. This is feasible in part thanks to the unique linguistic environment of Barcelona (Spain), where a large portion of the population is highly bilingual and is constantly exposed to the two co-official languages, Catalan and Spanish. Given that these two languages overlap substantially at both lexical and phonological levels, Spanish native speakers are predisposed to have a good level of Catalan comprehension. That having been said, some Spanish native speakers do not reach a high level of speaking in Catalan either because they began learning Catalan later in life or because native Catalan speakers speak Spanish as well. Thus, within this language context, Catalan native speakers typically have a language profile of early and high proficient bilinguals, whereas Spanish natives are more variable in terms of Catalan proficiency, age of acquisition and language usage. Thus, this linguistic variability produces several forms of bilingualism as defined by the multiple intersections between variables composing each individual's language history.

Second, in order to minimize the impact of potential confounding factors such as socio-cultural differences, we recruited all participants from the same city. Additionally, we assessed those factors that are known to significantly increase cognitive reserve and brain resilience, such as leisure activities, occupation, and education across an individual's lifespan.

Finally, we investigated the origin of bilingualism as a cognitive reserve factor via experimental measures of EC and long-term memory tasks. Indeed, some studies have highlighted the benefits of bilingualism in elderly people demonstrated within various tasks involving components of the EC system, such as attention (e.g., Bialystok, Craik, & Luk, 2008; Bialystok et al., 2004), working memory (Luo, Craik, Moreno, & Bialystok, 2013) and switching task abilities (Gold et al., 2013); this would suggest that the modulation of the EC abilities plays a potential role in delaying the onset of cognitive decline in bilinguals.

Several models describe the architecture of the EC system and adopt different views on its mechanisms and tasks to assess them (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Botvinick,

Cohen, & Carter, 2004; Diamond, 2013; Jurado & Rosselli, 2007; Norman & Shallice, 1986; Stuss & Alexander, 2000; Verhaeghen & Cerella, 2002). In our study, we adopted the EC model described by Miyake et al. (2000) which clearly defines three sub-components (inhibitory control, updating, and shifting) and suggests tasks associated with each of them. Updating mechanisms monitor the information during the task, shifting refers to the process that underlies the ability to switch between tasks, and inhibition suppresses prepotent non-target responses. Despite a recent revision of this framework, its general architecture has not changed dramatically. In the most recent version of the model (Miyake & Friedman, 2012), inhibition remains a crucial component of the EC system; however, it is now described as a more general factor that shares importance with updating and shifting.

The main hypothesis of the study is that higher degrees of bilingualism, as defined by early L2 acquisition, balanced language usage, higher L2 proficiency, and higher frequency of language switching would increase an individuals' cognitive reserve, as indicated by a delay of dementia and symptom onset as well as higher cognitive efficiency. Therefore, we expected a positive correlation between MCI and AD individuals' bilingualism composite scores and the clinical measures of age at onset of cognitive symptoms, at first clinical visit and at diagnosis. Similarly, at the cognitive level, we predicted that higher levels of bilingualism would positively correlate with the behavioural measures of EC and memory tasks (higher accuracy, reduced conflict/switch/mixing costs, and faster reaction times). Based on the previous studies in which a bilingual advantage was reliably found in older adults, we expected to find that the inhibitory control (Anderson et al., 2017; Bialystok et al., 2014) and updating (e.g., Gold et al., 2013; Grundy & Timmer, 2017) sub-components would be more strongly related to bilingualism. Finally, we argue that a bilingual advantage on EC would indicate that this cognitive system serves to compensate for the symptoms of cognitive decline, whereas an advantage on memory would be more related to an increase in efficiency of processes that counteracts the cognitive symptoms.

2. Methods

2.1. Participants

We recruited three groups of participants: 63 healthy individuals (M/F= 20/43), 135 patients with MCI (M/F= 62/73) and 68 patients with AD (M/F= 22/46). The patients were recruited from four different hospitals: Hospital de Bellvitge, Hospital de la Santa Creu i Sant Pau, Hospital General de Granollers, and Hospital Moisès Broggi (Sant Joan Despí/L'Hospitalet) - Consorci Sanitari Integral. Diagnoses were made by neurologists based on neurological and neuropsychological evaluations, according to the published clinical criteria. For AD, the clinical criteria were those based on the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease (McKhann et al., 2011). According to ICD-10 classifications, this corresponds to 'G30.1- Alzheimer disease with late onset,' defined as a decline with slow progression, with memory impairment as the principal feature and with an onset after the age of 65 (usually in the late 70s or thereafter). According to the DSM-V, our AD patients met the criteria for 'Major neurocognitive disorder,' with an insidious onset and gradual progression of impairment in one or more cognitive domains that interfere with their independence.

For MCI, the diagnosis was based on the recommendations of Albert et al. (2011), comprised of the following: lower performance in one or more cognitive domains including episodic memory, independence of function in daily life, and no evidence of significant impairment in social and occupational functioning. Single-domain and multiple-domain subtypes were classified as MCI only. All AD patients received acetylcholinesterase inhibitors as pharmacological treatment, whereas the MCI participants did not receive any medication for their diagnosis. According to ICD-10 classifications, this corresponds to 'F06.7 - Mild cognitive disorder,' which is characterized by the following: impairment of memory, learning difficulties, reduced ability to concentrate on a task for more than brief periods, marked feeling of mental fatigue, subjective feeling of difficulty in performing a cognitive task, and by having excluded a diagnosis of either dementia, delirium, or other mental and behavioural disorders. According to the DSM-V, our patients met the criteria for 'Mild neurocognitive disorder,' which is based on evidence of a modest cognitive decline compared to

previous levels of performance in one or more cognitive domains without interfering with independence in daily activities and having established that the cognitive deficits are not attributable to another mental disorder.

Patients with potentially confounding neurological (other than MCI or AD) and psychiatric disorders, clinically-known hearing or vision impairments, a past history of alcohol abuse, and/or psychosis were excluded from the study. Healthy individuals had no previous neurological or psychiatric diseases. Additionally, healthy individuals were excluded from the study if they showed signs of cognitive deficits on a brief neuropsychological assessment (see below).

2.2. Materials and procedure

For the purpose of the study, we collected clinical measures including age at onset of cognitive symptoms, age at the first medical visit for cognitive impairments, and age at diagnosis. Ages at the time of diagnosis and first visits were collected from the hospital records of the patients. Age at onset of cognitive symptoms was defined as the age of the patient when the first changes in cognition were observed by a reliable family member or as reported in the clinical records, if available. Language history and cognitive reserve measures were also collected for all participants. Finally, a brief neuropsychological battery was administered along with experimental measures: four EC tasks and a face memory recognition task detailed below.

Before starting the experimental procedure, the patients signed an informed consent approved by the 'Parc de Salut MAR' Research Ethics Committee under the reference number 2014/6003/I. The research was conducted in accordance with the Declaration of Helsinki (World Medical Association, 2013) and data protection procedures according to the General Data Protection Regulation 2016/679 (GDPR) of the European Union. The aims of the study were explained to participants at the beginning of the study and there was a debriefing with them after every experimental session.

2.2.1. Language history measures

Language history was assessed using a questionnaire administered to the participants and an interview with the patient and relatives (see Calabria et al., 2018). We excluded participants who spoke a third language as we aimed to focus our research on bilingualism.

Four main measures were collected (see Table 1):

a) Age of acquisition of the two languages (Catalan and Spanish);

b) Self-rating of language proficiency consisting of their speaking, comprehension, writing and reading abilities in each language on a four-point scale (1=poor, 2=regular, 3=good, 4=perfect);

c) Language usage represented by the frequency they spoke each of the two languages across different periods of their lives (childhood, puberty and adulthood); this was expressed as a percentage of Catalan usage, with 0% meaning only using Spanish throughout their lives, 100% meaning only using Catalan, and ~50% signifying a balanced use of the two languages.

d) Frequency of language switching as measured by the overall score on the Bilingual Switching Questionnaire (BSWQ) (Rodriguez-Fornells, Krämer, Lorenzo-Seva, Festman, & Münte, 2012).

The combination of all these measures was used to create a composite score of bilingualism (based on the results of a factorial analysis) which functioned a continuous variable ranging from passive bilingualism (being able to understand an L2, but with little or no usage of it) to active bilingualism (high proficiency in L1 and L2 with a balanced usage of the two languages).

2.2.2. Cognitive reserve index

To have a proxy of cognitive reserve apart from bilingualism, we used the Cognitive Reserve Index Questionnaire (CRIq) (Nucci, Mapelli, & Mondini, 2012). This includes 20 items that are grouped into three dimensions including factors of education, working activity and occupation, and leisure activity. This questionnaire yields a total score as well as three separate scores corresponding to each dimension: CRI-Education, CRI-Working Activity, and CRI-Leisure Time (see Table 1). Scores were calculated according the computation system provided by the authors of the CRIq, available at http://www.cognitivereserveindex.org/.

2.2.3. Neuropsychological measures

Patients were assessed with hospital-specific neuropsychological batteries that each collaborating hospital implemented for the diagnosis of cognitive decline. In order to establish a common set of test scores for all the participants, we designed a brief neuropsychological assessment specifically for this study that included: Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975); the CERAD Word List Memory (Morris et al., 1989), which measures long-term episodic verbal memory; forward and backward Digit Spans (Pena-Casanova et al., 2009), which measure verbal short-term memory; and the Trail Making Test part A (Peña-Casanova et al., 2009), which measures visual attention and motor speed (see Table 2).

TABLE 1 ABOUT HERE

2.2.4. Experimental tasks

All participants were tested on the five experimental tasks detailed below. Said tasks were administered over two sessions in no specific order. The four EC tasks included a flanker task (Calabria, Grunden, Serra, García-Sánchez, & Costa, 2019; Costa, Hernandez, & Sebastian-Galles, 2008), a Spatial Stroop task (Funes, Lupiáñez, & Milliken, 2007), a task switching task (Cattaneo, Calabria, Marne, Gironell, Abutalebi, & Costa, 2015) and an n-back task (Braver et al., 1997); the final task was a facial recognition memory task. All these tasks were administered to participants on a laptop computer and responses were collected with DMDX software (Forster & Forster, 2003). All the instructions for the experimental tasks were written on the screen and read by the participants before the task started. Additionally, the experimenter checked whether the participant correctly understood the instructions before running the task. After each session, there was a debriefing session with the participant.

Flanker task. Target stimuli consisted of a row of five horizontal black lines with arrowheads pointing left or right, with the central arrow acting as the true target. Participants were instructed to indicate the direction (left or right) of the central arrow by pressing one of two keys (‘V’ or ‘M’) on

the keyboard. The target (central arrow) was presented in two main conditions: with congruent flankers (same direction as the target) or incongruent flankers (opposite direction). The experiment consisted of two blocks of 48 trials each, for a total of 96 trials. The proportion of congruent trials was 75% (n= 72) to 25% incongruent trials (n= 24). The event presentation started with a fixation point (+) shown at the centre of the screen for 500 ms. Then, the target arrow was presented simultaneously with the flankers until the participants responded or for up to 2000 ms (for similar versions see Calabria, Grunden, Serra, García-Sánchez, & Costa, 2019; Costa, Hernandez, & Sebastian-Galles, 2008).

Spatial Stroop task. The stimuli consisted of an arrow that appeared on the left or right half of the screen. In the congruent condition, the direction of the arrow and its position on the screen was the same, while in the incongruent condition the direction of the arrow and its location was not the same (for instance, arrow pointing to left presented in the right-side part of the screen). The proportion of congruent/incongruent trials was 50%. The task consisted of 192 trials that were divided into four blocks of 48. Participants responded according to the left/right direction via pressing one of two keys ('V' if the arrow pointed to the right, 'M' if the arrow pointed to the right) on the keyboard (for a similar version of this task see Funes, Lupiáñez, & Milliken, 2007). The event presentation started with a fixation point (+) shown at the centre of the screen for 500 ms, which was followed by an arrow presented until the participants responded or for up to 2500 ms. This is an adapted version of the task used in the study by Funes, Lupiáñez, & Milliken, 2007).

Task switching. Three shapes (square, circle and triangle) and three colours (red, green and blue) were used in the task. Shapes and colour were combined in various ways, resulting in a total of nine possible coloured shapes. Participants were presented with an array containing three coloured shapes, two at the top and one at the bottom of the screen. They were instructed to match one of the coloured shapes at the top with the coloured shape at the bottom, according to the criteria of "colour" or "shape".

There were two types of blocks: single blocks and mixed blocks with a sandwich design such that participants completed two single blocks and 3 mixed blocks, followed by two more single blocks. In each single block (24 trials), the sorting criteria (shape or colour) was held constant; over a total

number of 96 trials, 48 single trials required sorting by shape and 48 single trials by colour. In the mixed blocks, however, participants had to sort the stimuli either by colour or shape according with the cue word appearing on the screen with the pictures. There were two types of trials: repeated trials in which participants had to use the same sorting criteria as in the previous trial and switch trials in which participants were required to match the coloured shapes in the opposite sorting criteria with respect to the previous trial.

Participants gave their response by pressing one of two keys ('M' or 'V') according to the position of the matching picture at the top of the array. Specifically, they had to press the 'M' key when the correct answer was in the top-right part of the array and the 'V' key when it was in the top-left part of the array. The criterion they had to use was indicated by a cue word appearing in the centre of the array for each trial ('COLOR' for colour, 'FORMA' for shape). The event presentation started with a fixation point (+) shown at the centre of the screen for 500 ms. Then, fthe cue word and the coloured shapes were presented simultaneously, remaining on the screen until the participants responded or for up to 2500 ms. This is an adapted version of the task that was used in the study by Cattaneo et al. (2015).

N-back task. Letters (consonants) were serially presented, and participants were required to match said letters in three different memory load conditions across separate blocks. In the 0-back condition, the target was any letter that matched a pre-specified letter (e.g., "X"); in the n-1 and n-2 back conditions, the target indicated when the letter on the screen matched the letter presented one or two trials before, respectively. There were three blocks of 25 trials containing 7 target trials (28%) and 18 no target trials (72%) in each. Target trials were never presented consecutively. Participants responded to every trial by pressing one key if the present stimuli matched the target or another if the stimuli did not match ('M' or 'V', counterbalanced across participants).

The event presentation started with a fixation point (+) shown at the center of the screen for 500 ms. Then, the stimuli were presented for a duration of 1500 ms or until the participants responded. The task was adapted for the version used in the study by Braver et al. (1997).

Face recognition memory task. The stimuli consisted of grey-scale pictures of faces that were downloaded from electronic datasets along with other resources on the web and then processed with

Adobe Photoshop 5.0. A set of 60 pictures of unfamiliar faces (half men and half women) was selected; they were scaled to 210 x 263 pixels and presented with a grey background.

During the encoding phase, a set of 30 pictures were presented twice and participants required to judge the attractiveness of the faces. The event presentation started with a fixation point shown at the center of the screen for 500 ms. Then, a face was presented during 3000 ms. Finally, the question "Attractive or not attractive?" was presented which remained visible up to 5000 ms. Participants responded to this question by pressing one of two keys on the keyboard ('V' or 'M'). This procedure was adopted in order to reinforce the creation of a memory trace during encoding. Moreover, participants were instructed to remember the encoded faces, since they were tested in a recognition memory task afterwards.

A recognition test was administered after a ten-minute delay. In this test all faces shown during encoding (old items) were presented along with an additional set of 30 that were not presented previously (new items). The event presentation started with a fixation point (+) shown at the center of the screen for 500 ms. Then, a face was presented until they responded or for up to 10000 ms. Participants had to indicate whether the face was presented previously during the encoding phase or not by pressing one of two keys on the keyboard ('V' or 'M').

3. Data Analyses

We performed separate stepwise multiple regression analyses on clinical measures (age at onset of cognitive decline, symptoms, and first visit) for the two patient groups and for the performance on each experimental task for both patients and healthy controls (Yaremko, Harari, Harrison, & Lynn, 1986). The regressors included in the analyses were the bilingualism composite factor, the cognitive decline composite factor and the CRIq score. Years of education were not included in the analysis since we had a similar measure (CRI-Education score) in the calculation of the total CRIq score.

The bilingualism composite factor was calculated by performing a principal component analysis (Jolliffe & Cadima, 2016; Sellbom & Tellegen, 2019). that included the following variables: years of language exposure to Spanish and Catalan (current participant's age – age of language acquisition); self-rating of language proficiency in both languages for speaking, comprehension, writing and

reading; percentage of language usage; and frequency of language switching (for a similar approach see Anderson, Hawrylewicz, & Bialystok, 2018).

Similarly, the composite score for the level of cognitive decline was calculated by performing a principal component analysis that included the scores obtained on the neuropsychological tests. We used all the neuropsychological measures together since using only the MMSE score might not have detected mild cognitive impairment (Carnero-Pardo, 2014; Diniz, Yassuda, Nunes, Radanovic, & Forlenza, 2007).

When the regressors showed a significant effect, partial correlation coefficients were calculated to determine the contribution of each predicting variable on the dependent variable (Freund, Wilson, & Mohr, 2010). Therefore, the square of each of these coefficients indicates the individual contribution of each predicting variable to the square of total R.

4. Results

4.1. Bilingualism composite factor

We ran a principal component analysis that included the following variables: years of Catalan exposure, years of Spanish exposure, percentage of language usage, frequency of language switching, fluency in Catalan, fluency in Spanish, comprehension in Catalan, and comprehension in Spanish. Reading and writing scores were not included in the analysis since most of the participants were only educated in Spanish, thereby generating possible language differences that could not be explained in terms of proficiency.

To improve internal consistency, we normalized the variable's scores by transforming them into z scores. After this transformation, the Cronbach's alpha reached .72 (Taber, 2018), indicating that internal consistency was acceptable (Tavakol & Dennick, 2011) and thus stipulating that the principal component analysis was appropriate for those variables. To correct for the common covariance of the variables, a rotation with the direct oblimin method was applied to the factor matrix.

After rotation, the result of the principal component analysis suggested that all the variables saturated into three factors, with a cutoff value of 1 for eigenvalues. The first factor included fluency

in Catalan (.93), language usage (.86), frequency of language switching (.83), comprehension in Catalan (.80), and years of Catalan exposition (.77). The second factor included fluency in Spanish (.73) and comprehension in Spanish (.73). The third factor only included the years of Spanish exposition (-.95). The results indicated that these three factors explained only 44% of the total variance.

One explanation of this low amount of explained variance is the fact that all the variables related to Spanish proficiency and exposure have low variability. This is reasonable since all Catalan-Spanish bilinguals have also acquired Spanish early in life (more or less at the same time as Catalan) and have a high level of proficiency in Spanish. Therefore, we ran a second principal component analysis that included the language variables for Catalan only (fluency, comprehension, and years of exposition), language usage, and frequency of language switching.

The internal consistency with this set of variables was excellent as suggested by a very high Cronbach's alpha of .90. The solution of this Catalan-based principal component explained 70% of the total variance and the variables saturated in one just factor. The component matrix showed the following loadings: fluency in Catalan (.93), language usage (.86), frequency of language switching (.86), comprehension of Catalan (.76), and years of Catalan exposition (.79).

Accordingly to this solution, the individual scores for bilingualism (hereafter, composite bilingualism scores) were calculated using a regression method in which positive coefficients were indicative of higher degrees of bilingualism and negative ones of low proficiency and usage of Catalan.

4.2. Cognitive composite factor

The test scores were transformed into z scores and subsequently underwent a reliability analysis. The analysis that included all variables showed a poor internal consistency (Cronbach's alpha= .55). A higher internal consistency (Cronbach's alpha= .76) was found when the following measures were included: MMSE score and CERAD scores for recognition and free recall.

The solution of the principal component analysis suggested that all the variables saturated into one just factor that explained 66.6% of the variance. To correct for the common covariance of the variables, a rotation with the direct oblimin method was applied to the factor matrix. After rotation,

the loadings of the factor were the followings: CERAD recognition (.56), CERAD free recall (.27), and MMSE score (.22).

Accordingly to this solution, the individual composite scores for cognition were calculated using a regression method in which positive coefficients indicated that cognition was within the normal range and negative ones below the normal range.

4.3. The effect of bilingualism on delaying cognitive symptoms

The results were consistent for three regression models for age at symptoms onset ($F (3, 189) = 10.15$, $p< .001$, $R^2= .14$), first visit ($F (3, 189) = 12.56$, $p< .001$, $R^2= .17$), and diagnosis ($F (3, 189) = 11.91$, $p< .001$, $R^2= .16$) (Table 2). That is, CRI score was not a significant predictor of the age at any time point (symptoms onset: $\beta= -.09$, $p= .24$; first visit: $\beta= -.12$, $p= 60$; diagnosis: $\beta= -.11$, $p= .16$), whereas both bilingualism and cognition as composite scores were. Cognition was a significant predictor of age at onset of symptoms ($\beta= -.29$, $p<.001$, $r=-.29$), of first visit ($\beta= -.29$, $p<.001$, $r= -.29$), and at diagnosis ($\beta= -.27$, $p<.001$, $r= -.28$). The degree of bilingualism was a positive predictor of the three age measures (symptoms onset: $\beta= .29$, $p<.001$, $r= .26$; first visit: $\beta= .33$, $p<.001$, $r= .31$; diagnosis: $\beta= .39$, $p<.001$, $r= .32$).

However, when the analyses were performed separately for the two groups of patients, the regression models were significant in MCI patients for the three dependent variables [age at symptom onset: $F (3, 124) = 11.49$, $p< .001$, $R^2= .22$; age at first visit: $F (3, 124) = 11.54$, $p< .001$, $R^2= .22$; age at diagnosis: $F (3, 124) = 12.18$, $p< .001$, $R^2= .23$], but not in AD patients [age at symptom onset: $F (3, 61) =.59$, $p= .63$, $R^2= .03$; age at first visit: $F (3, 61) = 1.14$, $p= .34$, $R^2= .05$; age at diagnosis: $F (3, 61) = 1.03$, $p= .38$, $R^2= .05$].

In MCI patients, both bilingualism and the degree of cognitive decline were significant predictors of the three age variables (see Figure 1 and Table 2 for partial correlations). Moreover, CRI significantly predicted, but in a negative direction, the age at onset of symptoms ($\beta= -.26$, $p= .01$) and age at diagnosis ($\beta= -.22$, $p= .03$).

As some research has shown that gender might be an important factor that modulates the prevalence of AD (Malpetti, Ballarini, Presotto, Garibotto, Tettamanti, & Perani, 2017; Rocca, 2017) and second language acquisition (van der Slik, van Hout, Schepens, 2015), we reran the regression

analyses with gender included as predictor. The results for the three regression models were still significant: age at symptoms onset (F (4, 188) = 7.93, p< .001, R^2= .14), first visit (F (4, 188) = 9.69, p< .001, R^2= .17), and diagnosis (F (3, 188) = 9.05, p< .001, R^2= .16). However, gender was not a significant predictor in any regression model: age at symptoms onset (β= .07, p= .27, r= .07), first visit (β= .07, p= .30, r= .07), and diagnosis (β= .05, p= .46, r= .05), suggesting that gender was not a modulating factor in delaying the symptoms of cognitive decline and unrelated to the effects of bilingualism.

TABLE 2 ABOUT HERE

FIGURE 1 ABOUT HERE

4.4. The effect of bilingualism on EC and memory

4.4.1. Flanker task

RTs and conflict cost. Regression models on RTs for the two conditions (congruent and incongruent) revealed that bilingualism was not a significant predictor (congruent: β= .02, p= .29, r= .06; incongruent: β= .06, p= .41, r= .05), but CRI (congruent: β= -.18, p= .01, r= -.16; incongruent: β= -.17, p= .01, r= -.16), cognition (congruent: β= -.24, p< .001, r= -.22; incongruent: β= -.32, p< .001, r= -.30), and age (congruent: β= .20, p= .002, r= .18; incongruent: β= .16, p= .01, r= .1) were.

Furthermore, an analysis was performed on the conflict cost as measured by the difference between RTs of the incongruent and congruent trials. To control for group differences in speed of processing, proportional costs were calculated, defined as the conflict cost divided by RTs of congruent trials. The regression model showed that cognition was a significant predictor (β= -.21, p= .002, r= -.20), but CRI (β= -.01, p= .94, r= -.01) and bilingualism (β= .07, p= .37, r= .06), and age (β= -.01, p= .87, r= -.01) were not (see Figure 2).

When gender was included in the analyses, the results showed that it was not a significant predictor in any regression model for RTs (congruent: β= .02, p= .72, r= .01; incongruent: β= -.01, p= .80, r= -.01) or conflict cost (β= -.005, p= .94, r= -.005).

Accuracy. The regression model for accuracy was significant (F (4, 228) = 15.87, p< .001, R^2= .20). Cognition (β= .37, p< .001, r= .34) and age (β= -.17, p= .01, r= -.15) were significant predictors, but bilingualism (β= -.07, p= .33, r= -.07) and CRI (β= .12, p= .08, r= .10) were not. When gender was included in the analyses, the results showed that it was not a significant predictor (β= .07, p= .27, r= .07).

4.4.2. Spatial Stroop task

RTs and conflict cost. Regression models on RTs for the two conditions (congruent and incongruent) showed that bilingualism was not a significant predictor (congruent: β= .10, p= .15, r= .08; incongruent: β= .05, p= .04, r= .08), but CRI (congruent: β= -.18, p= .01, r= -.15; incongruent: β= -.13, p= .05, r= -.11), cognition (congruent: β= -.24, p< .001, r= -.22; incongruent: β= -.29, p< .001, r= -.27), and age (congruent: β= .25, p< .001, r= .23; incongruent: β= .25, p< .001, r= .23) were.

Additionally, an analysis was performed on the conflict cost measured by the difference between the RTs of the incongruent and congruent trials. To control for group differences in speed of processing, proportional costs were calculated as the conflict cost divided by RTs of congruent trials. The regression model showed that bilingualism (β= -.20, p= .01, r= -.16), cognition (β= -.14, p= .03, r= -.13), and CRI (β= .19, p= .01, r= .16) were significant predictors but age was not (β= -.04, p= .55, r= -.03) (see Figure 2).

When gender was included in the analyses, the results showed that it was not a significant predictor in any regression model for RTs (congruent: β= .03, p= .57, r= .04; incongruent: β= .04, p= .69, r= .05) or conflict cost (β= .05, p= .77, r= .05).

Accuracy. The regression model for accuracy was significant (F (4, 233) = 14.29, p< .001, R^2= .20). Age (β= -.18, p= .004, r= -.19) and cognition (β= .34, p< .001, r= .32) were significant predictors, but bilingualism (β= -.11, p= .14, r= -.09) and CRI (β= .01, p= .96, r= .03) were not. When gender was included in the analyses, the results showed that it was not a significant predictor (β= .07, p= .24, r= .08).

4.4.3. Task switching

RTs, switch cost, and mixing cost. Regression models on RTs for the three conditions (single, repeat, switch) showed that bilingualism was not a significant predictor (single: β= .03, p= .71, r= .02; repeat: β= .05, p= .44, r= .04; switch: β= .07, p= .33, r= .06). CRI (single: β= -.23, p= .001, r= -.18; repeat: β= -.23, p= .001, r= -.19; switch: β= -.24, p= .001, r= -.20), age (single: β= .21, p= .001, r= .19; repeat: β= .19, p= .002, r= .18; switch: β= .23, p< .33, r= .22), and cognition (single: β= -.31, p< .001, r= -.28; repeat: β= -.29, p< .001, r= -.27; switch: β= -.30, p< .001; r= -.28) were significant predictors.

Additional analyses were performed on switch and mixing costs as two measures of cognitive control: reactive and proactive control, respectively (see Braver, 2012; Cattaneo et al., 2015). To control for group differences, proportional costs were calculated. Proportional switch costs were calculated as the difference between RTs in switch trials and repeat trials (mixed blocks) divided by RTs in repeated trials. Proportional mixing costs were calculated as the difference between RTs in repeat and single trials divided by RTs in single trials.

The regression models for both proportional costs were not significant (switch cost: F (4, 234) = 1.97, p= .10, R^2= .03; mixing cost: F (4, 234) = .73, p= .57, R^2= .01), suggesting that no regressor predicted the magnitude of these costs (see Figure 2).

When gender was included in the analyses, the results showed that it was not a significant predictor in any regression model for RTs (single: β= .03, p= .47, r= .03; repeat: β= .04, p= .68, r= .04; switch: β= .06, p= .30, r= .07), switch costs (β= .04, p= .56, r= .04) or mixing cost (β= .08, p= .21, r= .08).

Accuracy. The regression model for accuracy was significant (F (4, 234) = 13.47, p< .001, R^2= .15). CRI (β= .21, p= .004, r= .17), cognition (β= .25, p< .001, r= .24), and age (β= -.22, p= .001, r= -.21) were significant predictors, but bilingualism was not (β= -.05, p= .53, r= -.04). When gender was included in the analysis, the results showed that it was not a significant predictor (β= .02, p= .74, r= .02).

4.4.4. N-back task

The dependent variable of the regression analyses was composed of d' scores. These were calculated as the difference between the Z transformations of the percentages of hits and false alarms (d'= ZHit – ZFA) for n-0, n-1, and n-2 conditions separately. The percentage of hits was calculated as the proportion of correct responses over the total number of targets, and the percentage of false alarms as the proportion of false alarms over the total number of non-target trials.

The regression models were significant for the three memory load conditions (n-0: $F(4, 219) = 10.78$, $p < .001$, $R^2 = .16$; n-1: $F(4, 212) = 13.75$, $p < .001$, $R^2 = .21$; n-2: $F(4, 199) = 14.93$, $p < .001$, $R^2 = .23$). Bilingualism (n-0: $\beta = -.02$, $p = .79$, $r = -.01$; n-1: $\beta = -.07$, $p = .31$, $r = -.06$; n-2: $\beta < .01$, $p = .99$, $r < .01$) and age (n-0: $\beta = -.06$, $p = .38$, $r = -.05$; n-1: $\beta = -.01$, $p = .81$, $r = -.01$; n-2: $\beta = -.01$, $p = .06$, $r = -.10$) were not significant predictors of the n-back task performance. CRI (n-0: $\beta = .20$, $p = .009$, $r = .17$; n-1: $\beta = .22$, $p = .003$, $r = .18$; n-2: $\beta = .16$, $p = .05$, $r = .12$) and cognition (n-0: $\beta = .29$, $p < .001$, $r = .27$; n-1: $\beta = .36$, $p < .001$, $r = .33$; n-2: $\beta = .36$, $p < .001$, $r = .33$) were significant predictors (see Figure 2).

When gender was included in the analyses, the results showed that it was not a significant predictor in any regression model for the d' values (n-0: $\beta = .07$, $p = .25$, $r = .08$; n-1: $\beta = -.01$, $p = .083$, $r = -.01$; n-2: $\beta = -.02$, $p = .73$, $r = -.3$).

4.4.5. Face recognition memory task

The dependent variable of the regression analyses was defined as d' scores (d'= ZHit – ZFA). The percentage of hits was calculated as the proportion of correct responses (old items responded as 'old') over the total number of old items in the recognition memory task, and the percentage of false alarms (new items responded as 'old') as the proportion of false alarms over the total number of new items in the recognition memory task.

The regression model was significant: $F(4, 241) = 19.61$, $p < .001$, $R^2 = .25$). Bilingualism was not a significant predictor of the recognition memory performance ($\beta = .11$, $p = .10$, $r = .09$, (see Figure 2), but CRI ($\beta = .13$, $p = .05$, $r = .11$), cognition ($\beta = .29$, $p < .001$, $r = .27$), and age ($\beta = -.25$, $p < .001$, $r = -.24$) were.

When gender was included in the analyses, the results showed that it was not a significant predictor ($\beta = -.05$, $p = .34$, $r = -.06$).

FIGURE 2 ABOUT HERE

5. Discussion

In this study, we explored the relationship between bilingualism and CR by introducing some methodological novelties that challenge the traditional classification of monolingualism versus bilingualism and by employing experimental tasks with the intention of better characterizing the origin of the so-called "bilingual advantage" (Duñabeitia & Carreiras, 2015). Additionally, we controlled for other CR factors such as education, occupation and leisure activities, as they could potentially be related to bilingualism (Foubert-Samier et al., 2012; Fratiglioni, Paillard-Borg, & Winblad, 2004; Opdebeeck, Martyr, & Clare, 2016; Scarmeas & Stern, 2003; Stern, 2012). The main result of the study is a demonstrable and reliable effect of bilingualism in delaying the onset of cognitive symptoms and age of diagnosis in MCI patients. Such a bilingual advantage was only partially explained by a more efficient EC system and is not due to superior long-term memory in bilinguals.

One of the long-standing limitations of the research that has investigated the benefits of bilingualism on cognition has been the debate over how to establish a clear definition of bilingualism (Bak, 2016; Duñabeitia & Carreiras, 2015; Valian, 2015). To overcome this limitation, we decided to use a composite score of bilingualism, including several variables associated with the degree to which a given individual masters two languages and then calculating the specific weight of each component on a continuum, from passive to active bilingualism (for a similar approach, see Anderson et al., 2018). In our study, we showed that in the calculation of the bilingualism score almost all the variables contributed in a similar way to the continuum from passive to active bilingualism, with Catalan proficiency in speaking as the most important variable. Consequently, this result would support the idea that language proficiency may have more of an impact on determining a high degree of bilingualism than, for instance, age of L2 acquisition. This is not a new result, since some previous

studies had already found that language proficiency is one of the main components, together with language usage, in defining the degree of bilingualism as a continuous variable (Luk & Bialystok, 2013). However, it should be acknowledged that other variables can enhance an individual's degree of language proficiency and that this is not the only dimension that defines a person as a bilingual. For instance, individuals with early bilingual experience tend to also have higher L2 proficiency (Luk, De Sa, & Bialystok, 2011), despite the fact that in some cases these two variables can differently modulate the pattern of brain activation during lexical retrieval of the two languages (Perani et al., 2003). Also, language usage, more than language proficiency, modulates white matter in the brain areas related to language control, such as the anterior cingulate cortex (Del Maschio et al., 2019); in other cases, both language proficiency and age of L2 acquisition strongly predict the density of grey matter in the left inferior parietal cortex (Mechelli et al., 2004). Interestingly, beyond the realm of language, age of L2 acquisition and language proficiency have been shown to be the two main factors that enhance EC efficiency, as shown in tasks of conflict monitoring (Luk, De Sa, & Bialystok, 2011). This is to say that the combination of experience-based factors in using and knowing the two languages may shape the impact of related benefits (DeLuca, Rothman, Bialystok, & Pliatsikas, 2019), potentially ranging from an absence of effects in passive bilinguals to positive effects in active bilinguals with strong immersive language experience.

However, although we cannot definitively conclude which is the most relevant variable in determining a high degree of bilingualism, we found, as expected, a significant impact of active bilingualism in delaying the average age at symptom onset, first visit and diagnosis. The effect of bilingualism was found in MCI but not in AD patients (for reviews, see Calvo et al., 2016; Guzman-Velez, 2016). This result contributes to literature concerning the effect of bilingualism in MCI that was not consistently found in previous studies (Rosselli et al., Duncan et al., Ramakrishnan et l., Kowoll et el.).

The fact that bilingualism acts as a CR factor only within MCI patients could be explained by two main reasons, among others. First, it could be that the AD group lacked a sufficient level of power. Specifically, we had only 63 patients while there were more than double this amount in the MCI group; therefore, it might be the case that a larger amount of noise cancelled out any small effect

of bilingualism in the AD group while, in contrast, there was enough power in the MCI group to capture such an effect. Second, it could be that the protective effect of bilingualism in delaying the impact of disease acts only until a certain stage of pathology and then it reverses. Even if it is true that, according the neural reserve hypothesis, people with a higher level of CR may cope better with the symptomatology of cognitive decline despite having a larger amount of neuropathology, this might depend on the stage of the disease itself. According to this hypothesis (Stern, 2012), it is expected that bilingual AD patients would tolerate disease-related pathology more than monolinguals (or passive bilinguals), but their rate of decline over time would be faster than that of monolingual individuals. That is, once AD emerges, there is a point at which the underlying pathology is so severe that any possible cognitive advantage would no longer be maintained and individuals with both high and low levels of CR would show the same cognitive decline (Stern, Albert, Tang, & Tsai, 1999; Stern, Tang, Denaro, & Mayeux, 1995). Therefore, it might be the case that, in our sample, AD patients with a higher degree of bilingualism had already reached the point at which the neuropathology was severe enough to counteract the protective effect of speaking two languages (for a difference in brain atrophy patterns between MCI and AD in bilinguals and monolinguals, see also Duncan et al., 2018). Additionally, the null effect found in AD patients might be explained by the fact that the benefit associated with active bilingualism in our study was smaller than that reported by other studies, where monolinguals and bilinguals were compared. Previous studies with AD patients found a protective effect of bilingualism of 4-5 years (Alladi et al., 2013; Anderson, Saleemi, & Bialystok, 2017; Chertkow et al., 2010; Craik, Bialystok, & Freedman, 2010; Ossher, Bialystok, Craik, Murphy, & Troyer, 2013; Woumans et al., 2015; Woumans, Versijpt, Sieben, Santens, & Duyck, 2017; for a review Calvo et al., 2016); however, in our study it was reduced at about 2 years in MCI likely because we compared active and passive bilinguals. Therefore, the smaller effect found in MCI could have been undetected in the AD group, where the neuropathology had increased to such an extent that the positive effects of CR associated with bilingualism was not able to compensate for the presence of cognitive deficits.

Interestingly, the effect of bilingualism on delaying cognitive symptoms and the onset of diagnosis in MCI patients was independent from other CR factors such as occupation, leisure

activities and education. To measure the contribution of these factors on CR, we used a questionnaire (Nucci et al., 2012) that included items for all three dimensions. The results of the regression analyses did not show a positive effect on delaying the age of disease onset or cognitive symptoms for any of these CR contributors. Additionally, after controlling for these factors, our results showed that the effect of actively speaking two languages predicted age of onset (~.35) as well as cognitive decline (~.30). This adds a new piece of evidence into the debate surrounding the effect of bilingualism on dementia and it suggests a need to control for these other CR factors which were not controlled for in some prior studies. Moreover, we can exclude the possibility of immigration acting as a confounding variable in our sample, an issue faced in many studies concerning the effect of bilingualism on CR. In fact, our more active bilinguals were those that were native Catalan speakers and passive ones were immigrant individuals; in other words, the opposite situation existed in our study sample compared to the usual trend of bilinguals also being immigrants (e.g., Bialystok et al., 2007; Chertkow et al., 2010; Kowoll et al., 2016).

In replicating the effect of bilingualism on delaying cognitive symptoms and the age of diagnosis for MCI, the challenge still remains in explaining the origin of such an advantage in neurodegenerative diseases. In our study, we explored the underlying cognitive mechanisms by investigating individual performance on several EC and long-term memory tasks. The main reason behind focusing our research on EC came from extensive previous research in healthy individuals that found evidence of a bilingual advantage in this cognitive domain (e.g. in older adults Bialystok et al., 2004, 2008; for reviews see Lehtonen et al., 2018; Paap et al., 2015; Valian, 2015). The standing hypothesis is that bilinguals continuously use language control mechanisms to avoid cross-language interference and this lifelong training in control would transfer its benefits to domain-general cognitive processes, resulting in increased efficiency within the EC system (Prior & Gollan, 2013; Timmer, Calabria, & Costa, 2019). Therefore, one could expect that lifelong training of actively speaking two languages would be beneficial in counteracting the negative effects of cognitive decline in bilinguals. Indeed, some studies have demonstrated that EC networks in older bilinguals have higher neural efficiency than those of monolinguals (Gold et al., 2013; 2015; Luk et al., 2011) or are

less susceptible to disruption in bilingual individuals with dementia (Borsa et al., 2018; Perani et al., 2017).

The novel portion of our study was to include a set of EC tasks aimed at assessing three sub-processes defined by Miyake et al. (2000) as the main components of the system, namely switching, updating, and inhibitory control. According to the existing evidence of the bilingual advantage, we expected to see an effect of active bilingualism on the inhibitory control system, observed in older adults' performance on the flanker task, the Simon task and the ANT (e.g., Anderson et al., 2017; Bialystok et al., 2004; Bialystok & Craik, 2010; Goral et al., 2015). The evidence of a bilingual advantage in working memory is scarce, mostly because of the limited number of published studies involving older bilinguals (Grundy & Timmer, 2017). Similarly, the bilingual advantage in switching abilities remains controversial as it has been shown in few studies (Prior & Gollan, 2011; Prior & Macwhinney, 2010) and not always replicated (Hernández, Martin, Barceló, & Costa, 2013).

In the present study, although we did not find an effect of active bilingualism across all EC tasks, we did find a consistent effect in tasks classified as inhibitory control tasks according to Miyake and colleagues. The result of this "limited" bilingual advantage effect might be related to the fact that people who had a higher degree of bilingualism also showed a delay in the onset of cognitive symptoms. Therefore, one might expect no group difference in cognition since these individuals already have an advantage in terms of cognitive decline for its delayed onset. In most of the studies where bilingualism has been shown to be a CR factor, monolinguals and bilinguals were matched for the degree of cognitive impairment as a way of excluding potential differences between groups due to disease impact (Calvo et al., 2016). Thus, in order to find evidence of an advantage in EC, one should compare bilinguals and monolinguals who were diagnosed at the same age and see whether bilinguals outperform monolinguals in cognitive control tasks.

Nevertheless, the use of experimental tasks in our study aimed at providing more fine-grained measures (for instance, RTs) of cognitive system functioning and thereby better capture individual differences. The results showed that participants with higher degrees of bilingualism exhibited a lesser conflict cost than those with passive bilingualism and, similar to other findings, the bilingual advantage on the spatial Stroop task was independent from other CR factors measured with the CRI.

The question as to why active bilinguals outperformed passive ones only in this task may have an explanation within the bilingual language control system. According to Green and Abutalebi (2013), eight different processes are involved in bilingual language control, but three of them are highly engaged in individuals who actively speak their two languages in the same context: goal maintenance, conflict monitoring and interference suppression. Goal maintenance is required to maintain the activation of one language while the other two processes are necessary for avoiding cross-language interference from the non-intended language. Additionally, for accurate selection of a new language when required by the context, interference suppression would modulate the activation/inhibition of the other language. According to Green and Abutalebi (2013), all these processes are strictly related to the inhibitory control needed for the selection of the output, as much in one language as in the other. Interestingly, this cognitive perspective complements the findings that domain-general areas of conflict monitoring are also involved in response selection in bilinguals (Branzi, Della Rosa, Canini, Costa, & Abutalebi, 2016). Neural models of bilingualism (Abutalebi & Green, 2008; Calabria, Costa, Green, & Abutalebi, 2018) have also proposed that more anterior areas of the brain, including the anterior cingulate cortex and prefrontal cortex, are typically active during language switching and language selection tasks, especially when bilinguals are placed in dual-language circumstances (Abutalebi & Green, 2016; Borsa et al., 2018). Interestingly, the anterior cingulate cortex is also involved in conflict and error monitoring tasks within EC (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999) and bilinguals use this structure more efficiently than monolinguals to monitor non-linguistic conflicts (Abutalebi et al., 2012).

Therefore, according to these findings, we might speculate that more efficient non-linguistic processes of conflict monitoring in active bilinguals, via inhibitory control, may contribute to compensation of cognitive decline symptoms and, in turn, delay their onset. The fact that the bilingual advantage was not found in the flanker task most likely means that the benefits rely more on the response selection rather than at the stimulus interference level. Indeed, to solve the conflict in the spatial Stroop task, individuals needed to be more efficient at solving the incompatibility between the location of the stimulus and the response. This incompatibility is not present in the flanker task, but it is for language selection and, consequently, inhibitory control is enhanced in bilinguals who switch

more and actively use both languages. Finally, active bilinguals did not outperform passive ones in the long-term memory tasks, as found in some studies that contrasted bilinguals and monolinguals with neurodegenerative diseases (Perani et al., 2017; Rosselli et al., 2019). This means that the delay of cognitive symptoms of MCI patients is not completely explained by a protective effect originating from a more efficient memory system. One of the hypotheses of the underlying mechanisms of CR is that individuals with higher levels of CR would be protected from the negative effects of the neuropathology because they have developed a more efficient memory system (Barulli & Stern, 2013; Scarmeas & Stern, 2003; Stern, 2012; Stern et al., 2018). A better memory would give them a higher threshold for receiving a diagnosis of dementia and thus high-CR individuals would be diagnosed later compared to individuals who have lower levels of CR. This is one of the possible hypotheses that we proposed to explain the bilingual advantage, since recent findings have shown that memory-related areas could be less impacted by the effects of aging in people who speak two languages (Heim et al., 2019). Moreover, Grant et al. (2014) proposed that the posterior-to-anterior shift of brain activity observed in monolingual older adults while they performed memory tasks (Davis et al., 2008) is not expected in bilinguals. Instead, bilinguals would show a preservation of the brain activity in the posterior regions, thus allowing them to have a more efficient memory and to be protected against cognitive decline. However, our results do not support the view of a more efficient memory system in active bilinguals versus passive bilinguals, at least concerning the capacities we tested, such as non-verbal memory.

However, our study has some limitations. First, we were not able to find a positive effect of bilingualism in AD, as has been previously reported in other studies (for a review Calvo et al., 2016). While we were able to provide some plausible explanations of this null effect, we have to acknowledge that the lack of statistical power for a smaller sample size might explain why active and passive AD bilinguals had a similar age at the onset of symptoms, first visit, and diagnosis. Accordingly, the results from MCI patients are more reliable given that the sample was larger.

Second, we failed to find an effect of gender on CR benefits associated with bilingualism. Some studies have highlighted that the gender is a relevant variable in the prevalence of AD (Malpetti et

al., 2017) and L2 acquisition (van der Slik et al., 2015). In our study, the number of female and male individuals was balanced within the two patient groups and this might have hidden an effect of gender in delaying the cognitive decline and modulating task performance. Indeed, it has been shown that women are disproportionally more affected with AD than men (Mielke, Vemuri, & Rocca, 2014) and this factor should be into account since it might modulate the magnitude of CR benefits (Rocca, 2017). Therefore, the fact that we used a balanced number of men and women in patient groups might have limited the possibility of finding a modulatory effect of gender on CR and bilingualism.

Finally, some studies have highlighted that the self-rating of language proficiency is not always a reliable measure of bilinguals' true language proficiency (MacIntyre, Noels, & Clément, 1997; Marian, Blumenfeld, & Kaushanskaya, 2007). In our study, we only used self-ratings and we acknowledge that this method might have captured some subjective distortions of their perceived language proficiency.

Nevertheless, these limitations can help to shape the future directions of research on bilingualism and CR. First, future studies should consider bilingualism as a continuous measure instead of comparing monolinguals and bilinguals as categorical variables. This method allows us to define the relative influence of each linguistic dimension of bilingualism on relative cognitive advantage. In the same vein, objective measures of language proficiency should be adopted, allowing studies to overcome the problem of reliability in subjective measures (Tomoschuk, Ferreira, & Gollan, 2019). Second, future research should explore the effect of bilingualism on CR with longitudinal studies (Costumero et al., 2020). Studying how bilingualism benefits individuals with neurodegenerative diseases over time is crucial for testing the CR hypothesis (Stern, 2012). According to this hypothesis, the benefits of CR should last until a certain degree of neuropathogoly is reached and then, beyond such a threshold, a slopper decline in cognition should be observed in patients with higher CR compared to those with lower CR. The research on the long-term benefits of speaking two languages could also add evidence to this

hypothesis. Third, future research should investigate the effect of bilingualism in other pathologies, such as Parkinson's or Huntington's disease (Calabria, Cattaneo, & Costa, 2017). These two pathologies are good candidates since they primarly affect EC processes and we know that EC is intimately related to bilingual language control. Because this relationship is the supposed origin of the bilingual advantage (Abutalebi & Green, 2016), we should expect a more consistent advantage on EC measures for bilingual patients with Parkinson's or Huntington's disease compared to other bilingual patients with less pathological affectation of EC functions.

In conclusion, our results replicate previous findings that speaking two languages may delay the cognitive symptoms of MCI. Moreover, we were able to show that the effect of bilingualism was independent from other CR factors such as education, leisure activity, and occupation. Additionally, we suggest the use of a bilingual composite score as a better way to reduce the impact of potential socio-cultural group differences when comparing bilinguals to monolinguals.

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Figure captions

Figure 1

Partial regression plots for the effect of bilingualism on age at symptom onset, first visit, and diagnosis.

Figure 2

Partial regression plots for the effect of bilingualism on the performance on EC and memory tasks.

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Table 1

Descriptive statistics for socio-demographic variables, language profile, and CRIs for AD patients, MCI patients and healthy controls

	AD patients			MCI patients			Healthy controls		
	n=68 (M/F= 22/46)			n=135 (M/F= 62/73)			n=63 (M/F= 20/43)		
	Mean	***SD***	***Range***	***Mean***	***SD***	***Range***	***Mean***	***SD***	***Range***
Age at onset of symptoms	72.9	5.2	63-85	70.5	5.5	58-85			
Age at first visit	74.4	5.0	63-87	71.4	5.5	59-85			
Age of diagnosis	75.5	5.3	63-87	73.1	5.2	59-87			
Age at testing	76.5	5.1	66-87	74.1	5.1	63-87	73.7	7.0	60-90
Education (years)	7.7	4.0	0-18	7.4	5.1	0-18	7.9	3.9	0-18
CRI-Education	95.4	19.4	43-148	96.7	16.5	67-153	101.4	16.6	65-154
CRI-Working Activity	92.7	21.1	66-157	89.9	16.1	66-139	94.0	19.1	71-184
CRI-Leisure Time	100.0	20.4	43-166	96.9	22.1	60-165	114.9	18.4	82-165
CRI-Total	95.4	18.6	71-150	92.7	19.4	63-149	104.4	17.6	79-160
Catalan									
Fluency (1-4)	2.7	1.4	1-4	2.5	1.4	1-4	3.2	1.2	1-4
Comprehension (1-4)	3.6	.7	1-4	3.5	.8	1-4	3.8	.6	1-4
Reading (1-4)	2.8	1.2	1-4	3.0	1.2	1-4	3.5	.9	1-4
Writing (1-4)	1.6	.9	1-4	1.7	1.1	1-4	2.2	1.1	1-4

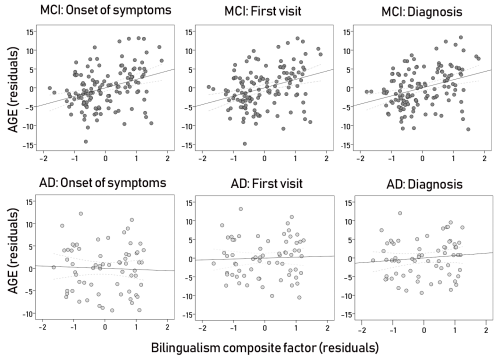
Spanish									
Fluency (1-4)	3.9	.2	3-4	3.9	.12	3-4	3.9	.21	3-4
Comprehension (1-4)	3.9	.4	3-4	4.0	-	4-4	4.0	-	4-4
Reading (1-4)	3.9	.4	2-4	3.9	.32	2-4	3.2	.13	3-4
Writing (1-4)	3.6	.7	2-4	3.5	.73	2-4	3.9	.37	2-4
Years of Catalan	63.6	16.3	10-87	60.4	14.1	19-87	66.2	12.8	40-90
Years of Spanish	74.6	5.1	63-87	72.5	2.5	58-87	72.0	6.6	58-87
Language usage (%)	24.1	22.9	0-64	22.9	24.2	0-66	27.4	20.9	0-61
Language switching score	16.2	12.5	0-35	14.11	12.2	0-37	20.2	12.2	0-35

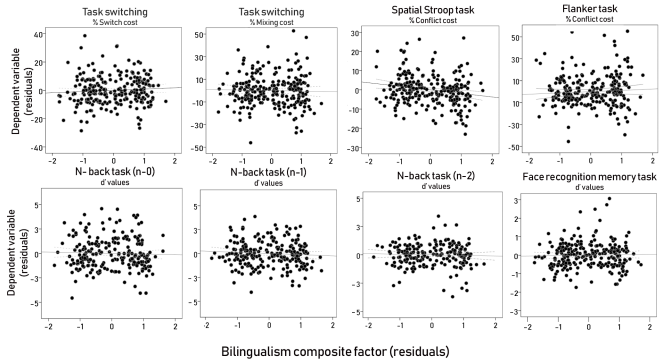
Table 2

Results of the multiple regression analyses and partial correlation coefficients between socio-demographic variables and CRI scores, bilingualism and neuropsychological assessment for MCI and AD patients.

Dependent Variable		Independent variables	B	Beta	t	p	Partial
Age at symptoms	***MCI***	Bilingualism factor score	*2.23*	*.41*	*4.44*	*<.001*	*.35*
	R^2 = .20	Cognitive factor score	*-2.83*	*-.29*	*-3.65*	*<.001*	*-.29*
		CRI score	*-.07*	*-.23*	*-2.49*	*.01*	*-.20*
	AD	Bilingualism factor score	.13	.02	.17	.86	.02
		Cognitive factor score	-.46	-.07	-.54	.74	-.07
		CRI score	.05	.15	1.14	.26	.14
Age at first visit	***MCI***	Bilingualism factor score	*2.31*	*.42*	*4.56*	<.001	*.36*
	R^2 = .19	Cognitive factor score	*-.82*	*-.29*	*-3.60*	*<.001*	*-.28*
		CRI score	-.05	-.16	-.171	*.09*	-.14
	AD	Bilingualism factor score	.62	.12	.86	.39	.11
		Cognitive factor score	-.19	-.03	-.22	.82	-.03
		CRI score	.05	.16	1.24	.22	.15
Age at diagnosis	***MCI***	Bilingualism factor score	*2.21*	*.42*	*4.60*	*<.001*	*.36*
	R^2 = .20	Cognitive factor score	*-2.80*	*-.30*	*-3.78*	*<.001*	*-.30*

	CRI score	*-.06*	*-.21*	*-2.25*	*.03*	*-.18*
AD	Bilingualism factor score	.86	.18	1.25	.21	.15
	Cognitive factor score	-.05	-.01	-.07	.94	-.01
	CRI score	.02	.09	.65	.52	.08





Highlights

- We tested whether active bilingualism may protect against cognitive decline.
- We tested patients with different degrees of language experience and usage.
- We collected clinical measures and performance in executive control tasks.
- Active bilingualism was a predictor of delay in the age at onset only in MCI.