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BILINGUALISM AS A CONTRIBUTOR TO COGNITIVE RESERVE IN HEALTHY AND PATHOLOGICAL AGEING

Albert Costa Martínez
Centre del cervell i cognició
César Ávila River
Facultat de ciències de la salut / Universitat Jaume I

1. Summary of the project

One question that has long captured the interest of neuroscientists is how the currently unavoidable cognitive deterioration associated with dementia can be delayed. For instance, great efforts have been invested in determining which environmental factors are behind individual differences in susceptibility to age-related decline (Fratiglioni et al., 2004; Rovio et al., 2005). One of the neuroscientific research priorities is to understand how some individuals develop so-called "cognitive reserve" (CR) mechanisms that make their brain more resilient when faced with dementia (Steffener and Stern, 2003; Stern, 2012). Epidemiologic studies indicate that, among other factors, higher educational level, mental activity, and cognitively demanding occupations protect individuals from the symptoms of dementia (Scarmeas and Stern, 2003; Scarmeas et al, 2001). More recently, research has shown that one of the environmental factors that promotes CR is also *bilingualism* (Byalistok, Craik & Luk, 2012). The general objective of the project was to *explore the cognitive and neural aspects of bilingualism as a factor contributing to CR in older people with and without cognitive decline.* The research involved three groups of participants of Spanish-Catalan bilinguals with varying degrees of bilingualism: healthy elderly adults, patients with a diagnosis of Mild Cognitive Impairment (MCI), and patients with probable Alzheimer's disease (AD).

This general aim of this project was divided in two specific parts:

1) *The relevant variables that might modulate the CR associated with bilingualism.* It has been established that bilingualism involves many different dimensions and there is some evidence suggesting that certain characteristics (age of second language (L2) acquisition, the proficiency of the L2, the use of two languages) may play a role in the extent to which the benefits of bilingualism on executive control (EC) are present both at behavioural and neuroanatomical level. Thus, the proposed question was to define the crucial variables related to bilingualism that might modulate the CR.

2) *The underlying mechanisms of how lifelong experience of using two languages protects against age-related diseases.* At least two main mechanisms have been proposed to explain CR: one is a suggested fortification of the brain areas that are affected by ageing and dementia by increasing their efficiency (neural reserve) while

the other theory involves the recruitment of alternative and spared networks (neural compensation). In the context of bilingualism, it is still an unresolved question as to how exactly CR acts both at the behavioural and the neural level. At neural level, we have evidence that in bilingual older adults there is an increase of the efficiency of some brain areas, whereas in bilingual AD patients there is evidence of a neural compensation mechanism. In this case, the question was to see which of these two mechanisms protect bilinguals against age-related diseases.

The project was jointly carried out by the Pompeu Fabra University and Jaume I University in collaboration with several hospitals in Catalonia and Valencia. The collaborators were: Hospital of Bellvitge (L'Hospitalet de Llobregat), Hospital de la Santa Creu i Sant Pau (Barcelona), Hospital de Sant Joan Despí Moisès Broggi - Consorci Sanitari Integral (L'Hospitalet de Llobregat), Hospital de Dia Sant Jordi (Granollers), Hospital General de Valencia, and Hospital La Fe (Valencia).

In order to achieve the above-stated objectives, the project was divided into three studies:

Study 1. The main aim here was *to investigate the modulation of the variables related to bilingualism on CR at behavioural level.* To define the degree of bilingualism, we used specific variables known to influence bilingual benefits in young adults and patients, such as age of L2 acquisition and L2 exposure, language proficiency and language switching rate. All these measures were collected through a language history questionnaire and a bilingual switching questionnaire (BSWQ) (Rodriguez-Fornells et al., 2012).

Participants were tested in several tasks that tapped into different cognitive domains such EC, attention and long-term memory. Specifically, we employed the following tasks: a) a spatial Stroop and Attentional Network task, for measuring attention; b) a non-verbal N-back task, for measuring working memory; c) a non-linguistic switching task, for measuring EC; and d) a face recognition memory task, for measuring long-term episodic memory.

In addition, to evaluate the degree of cognitive decline in patients we will include several neuropsychology measures. Finally, we will also evaluate the effect of

education, working activity and leisure time as contributors to CR with the Cognitive Reserve Index Questionnaire (CRIq, Nucci, Mapelli & Mondini, 2012).

Study 2. The main aim of the neuroimaging study was *to investigate the neural network related to bilingual advantage in CR.* To do so, we made use of different measures of structural and functional neural changes (morphometric, volumetric, and resting-state measures) in bilingual older adults, patients with MCI and with AD. The neurological measures were compared between two groups of participants: one with high degree of bilingualism (active) and one with low degree of bilingualism (passive). The study was conducted in a cross-sectional manner by comparing the two groups of bilinguals as well as longitudinally within one sub-sample of participants.

Study 3. This part of the project was intended to *investigate whether the bilingual advantage in EC would be causally related to the use of two languages in dementia*. To investigate this, participants were trained with various tasks of bilingual language production and control with the aim of improving the efficiency of the EC system. MCIs with low level of bilingualism (passive) were trained during two months at the Hospital de Bellvitge. The efficacy of the training was measured by testing participants before and after training on various cognitive tasks (the same tasks found in Study 1). Improvement in EC was measured by comparing one group that received the language training to another group with no training between pre/post measures but was in a waiting list to be trained afterwards.

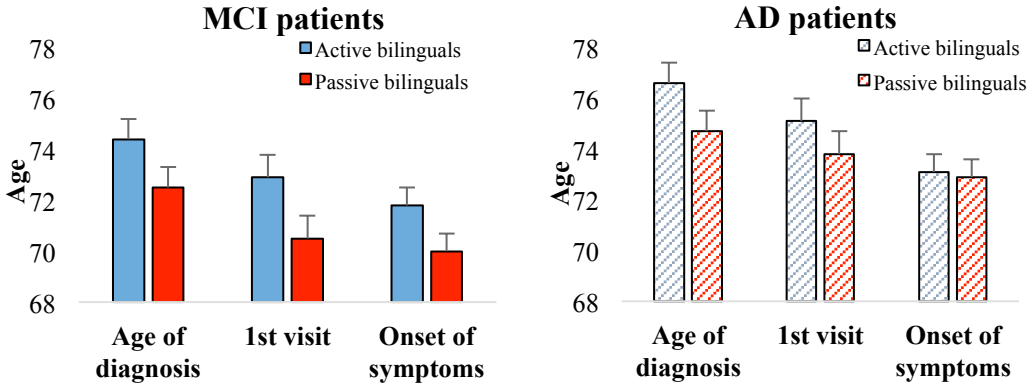
2. Results

Study 1. Active bilingualism delays the symptoms of cognitive decline and improves compensatory EC mechanisms

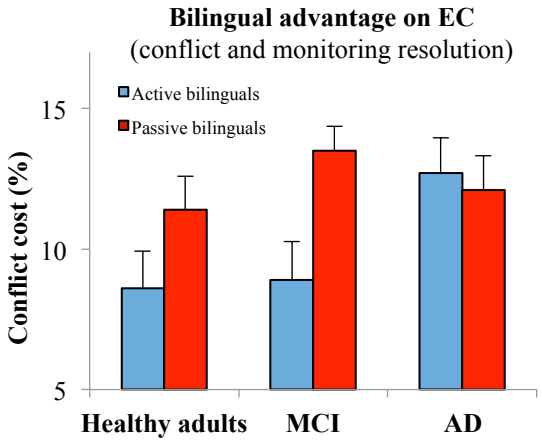
290 participants were recruited for Study 1 (80 patients with AD, 140 patients with MCI, and 70 healthy controls). Participants were classified as active (high frequency of Catalan usage along with early acquisition and high proficiency in both languages) or passive (low frequency of Catalan usage and low proficiency in both languages) bilinguals. The two groups were comparable based on neuropsychological scores across several tests of cognitive deficits.

Bilingual advantage on clinical variables. The analysis was conducted to compare passive vs. active bilinguals and showed that in both patient groups (AD and MCI) the active bilinguals had an advantage over passive ones in age of diagnosis and first clinical visit. No difference between these two groups was found for the onset of cognitive symptoms. The bilingual advantage ranged from 2 to 3.5 years, similar to what has been reported in some of the epidemiological studies on bilingualism and CR.

Bilingual advantage on age of testing, diagnosis, and first visit of active over passive bilinguals



Bilingual advantage on experimental tasks (EC, attention and memory). The analysis showed that, on EC task but not episodic memory tasks, individuals classified as active bilinguals performed better than passive ones. This result suggests that the underlying mechanisms of bilingualism as factor contributing to CR, at least in age-related disorders, are not linked to memory efficiency, one of the most affected cognitive processes in decline associated with Alzheimer's disease. A further result is that the advantage in EC was not observed for all the domains tested but rather specific to one task (Spatial Stroop) which implicates *conflict and monitoring resolution.* Moreover, the magnitude of the bilingual advantage in EC correlated with the age of acquisition of Catalan, suggesting that the earlier bilinguals started to speak a second language, the greater this advantage would become (see correlation below).

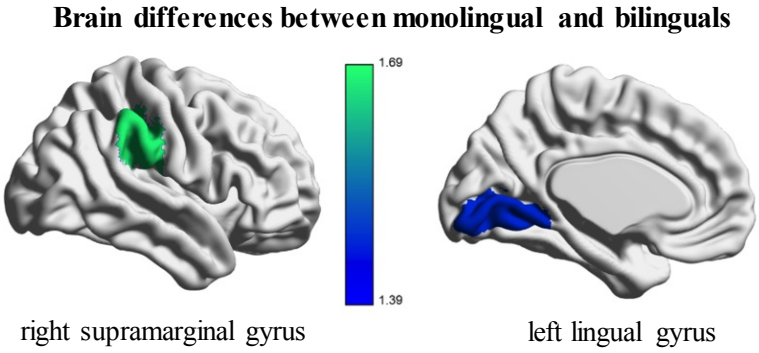


To summarize, the results of Study 1 show that *early L2 acquisition and active bilingualism delay the symptoms of dementia even in its preclinical stage (MCI), and this advantage was independent of years of education and other cognitive reserve factors*.

Study 2. Bilinguals' brains are more resilient to AD neuropathology.

163 participants were studied as part of Study 2 (36 patients with AD, 99 patients with MCI, and 28 healthy controls). Participants were classified as Catalan-Spanish bilinguals or Spanish monolinguals (high frequency of Catalan usage and high proficiency in both languages) bilinguals.

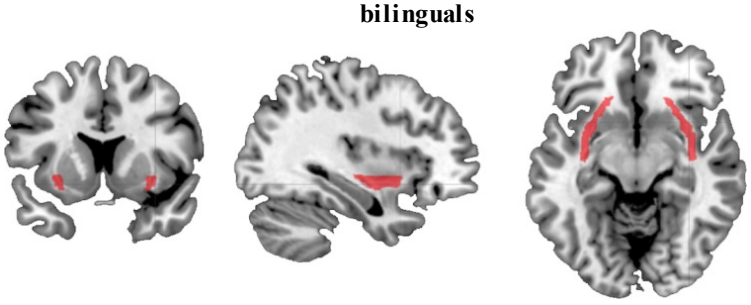
Cross-sectional study. The two designated language groups were comparable based on neuropsychological scores for several tests of cognitive deficits and were matched for age and years of education. Supporting our original hypothesis, global differences in brain parenchyma volume showed an overall reduction in brain volume in bilinguals, compared to monolinguals. In a further analysis, these neuroanatomical differences were more prominent within the right supramarginal gyrus and the left lingual gyrus. In a diffusion tractography analysis, bilinguals, compared to monolinguals, showed higher levels of atrophy in the fornix. Additionally, we found that monolinguals had a higher level of white matter atrophy in the left parahippocampal cingulum compared to bilinguals. Further comparing the two groups, a decreased resting state functional connectivity was observed in monolinguals between the right inferior frontal opercular and left precuneus as well as between the left precuneus and right inferior frontoparietal.



Longitudinal study. At a cognitive level, monolinguals showed a higher decline at follow-up compared to bilinguals, especially on phonemic fluency tests. At neural level, bilinguals showed a slower parenchymal volume loss compared to monolinguals across the time points. Using a more liberal threshold of $p<0.05$ uncorrected, we found significant differences between language groups in the right cingulate gyrus, right putamen right caudate, right hippocampus, and left fusiform gyrus.

Also, we found a higher rate of decline or deterioration in functional anisotropy in the bilateral inferior fronto-occipital fasciculus (IFOF) in monolinguals compared to bilinguals. However, no significant differences were found between bilinguals and monolinguals in longitudinal changes of resting state functional connectivity.

More white matter decline over time for monolinguals compared to bilinguals



Bilateral inferior fronto-occipital fasciculus

To summarize, the results of Study 2 show that *bilinguals, compared to monolinguals, can better tolerate the neuropathology associated with cognitive decline associated with Alzheimer's disease*. The language group differences at the neural level suggest that CR in bilinguals can be explained in terms of *compensatory mechanisms developed via lifelong production and control exerted over two languages.*

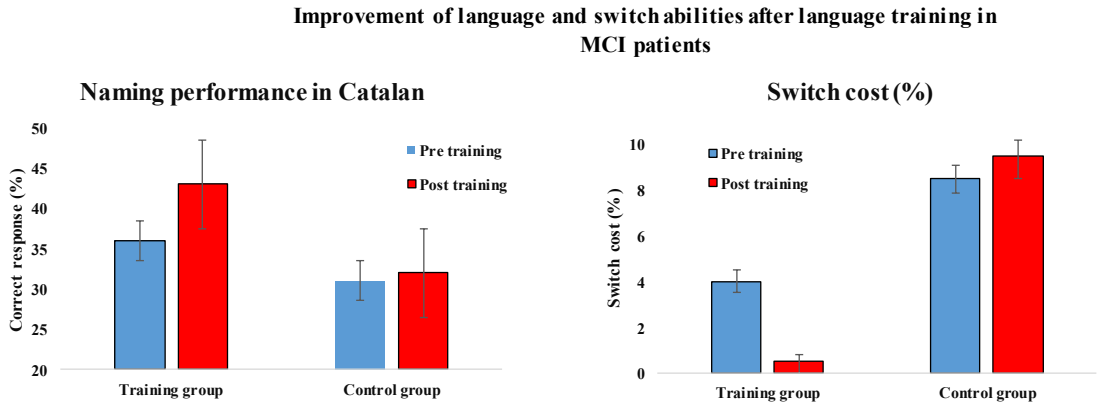
Study 3. Preliminary evidence of the benefits of language training on EC.
Over the course of two experiments, we studied EC benefits in language control (healthy young adults) and language learning (MCI patients).

Language control training in healthy young adults. Two groups of bilinguals were assigned to two different protocols: one group was trained in language switching (switching-task training group) and the other group was trained in blocked language picture naming (single-block training group). To test EC benefits, both groups performed a non-linguistic switching task before (pre-training) and after training (post-training). We found that the switch cost was smaller during the post-training task only

for the switching-task training group only. Therefore, because language switching training reduced the switch cost in a non-linguistic switching task, it was concluded that training effects can be transferred from linguistic to non-linguistic domain of control.

Language training in MCI patients. Twenty-three people with an age range between 65 and 81 years old and with a basic knowledge of Catalan (passive bilinguals) participated in the language training. One group (n=12) was trained during two months while a second group (n=11) was in a waiting list for training. This latter group served as a control/baseline group for the sake of this experiment and only received the language training after assessments were completed. Language training consisted in 16 sessions (2 per week) in Hospital de Bellvitge and pre- and post-training assessment of EC was performed.

We found that after language training participants improved their naming performance, suggesting that they acquired more vocabulary in Catalan. This result indicates that language abilities related to lexical retrieval can be enhanced in MCI patients and especially in a second language. Moreover, there was a marginally significant result for task switching after the first training. That is, MCI patients who received training performed better in task switching (reduction of switch cost) compared to control group. This an intriguing result because it suggests that language training may transfer its benefits to EC, in line to what we expect for the bilingual advantage for non-linguistic control.



3. Relevance and possible clinical applicability of final results

The results of the current project have several implications at the clinical level for bilingual people with cognitive decline:

1. *The active use of the two languages is a contributing factor to CR, aiding to protect against the onset of the cognitive decline.* By now, it has been shown that several lifestyle factors such as social activity, education level, and physical activity have the potential to ward off the cognitive symptoms of dementia. Here, we propose that, viewing bilingualism as one of these protecting factors, the active use of two languages serves as a mechanism promoting cognitive reserve. Through continuous switching between two languages and the monitoring required to control this executive function, bilingualism can strengthen other non-linguistic processes over a lifetime and increase an individual's cognitive efficiency. This higher efficiency of the EC in active bilinguals in turn can compensate the symptoms of cognitive decline and delay the onset of dementia. Moreover, this explanation is supported by the neural results of the project: brain areas showing grey matter differences related to the use of language were those traditionally associated with language control in bilinguals. That is, the increase of the neural efficiency in bilinguals could compensate for the negative effects associated with AD neuropathology. *This result has an impact at a diagnostic level, where clinicians need to consider bilingualism as one of the factors that delay the onset of cognitive symptoms.*

2. *The language abilities might deteriorate more in active than passive bilinguals.* We found that, when we compared the two groups of bilinguals in picture naming, active bilinguals performed worse than passive ones in their dominant language. This is known as bilingual disadvantage in language and can be explained by the fact that bilinguals use one language less frequently (compared to monolinguals), resulting in more difficulties during lexical retrieval. In support of this notion, we found a positive correlation between the accuracy of naming and the age of acquisition of the non-dominant language. That is, the earlier bilinguals acquire their non-dominant language, the greater the impairment in their ability to retrieve words in dominant is. This is a new finding in individuals with MCI and thus has a direct impact on clinical practice. Specifically, this highlights the importance *of testing verbal abilities in bilinguals by taking into account potential difference from monolinguals,* in order to avoid false

positives in the diagnosis of cognitive decline. Moreover, it highlights the need *to have normative data for bilinguals undergoing language assessment as they might score differently than monolinguals.*

3. The results from brief language training indicate new ways to conceptualize cognitive therapy. The positive effect of language training on EC that we found in healthy, young individuals suggests that the same procedure should to be tested in older adults and patients with cognitive decline. The results are promising and open the possibility of *training people in a new language with generalized positive effects on non-linguistic control processes.* The evidence that these two domains of control overlap opens new ways of implementing cognitive training by way of including language as one of the cognitive abilities that can be trained.

4. Efficacy of language training for improving vocabulary. MCI patients with passive knowledge of Catalan that were trained to use Catalan showed improvements in their vocabulary after 2 months. This is an important result given the limited number of studies with language learning in older adults and people with MCI. Therefore, we can conclude that *training a second language can help prevent language decline in more advanced stages of the disease*. There is also the possibility that a more intensive and/or longer intervention with language training would transfer its benefits to non-linguistic abilities, as we have seen in the study with young bilinguals.

4. Publications

Timmer K., Calabria M., & Costa A. (2019). Non-linguistic effects of language switching training. *Cognition*, 182, 14-24.

Calabria M., Baus C., & Costa A. (2019). Cross-talk between bilingual language control and executive control. In *The Handbook of the Neuroscience of Multilingualism*, W. Schwieter (Ed.), Wiley-Blackwell Press.

Calabria M., Costa A., Green D., & Abutalebi J. (2018). Neural basis of Bilingual Language Control. *Annals of the New York Academy of Sciences*, 1426, 221–235.

Calabria M., Cattaneo G., & Costa A. (2017). It is time to project into the future: a Special Issue on bilingualism in healthy and pathological aging. *Journal of Neurolinguistics*, 43, 1-3.

Calabria M., Cattaneo G., Marne P., Hernández M., Juncadella M., Gascón-Bayarri J., Sala I., Lleó A., Ortiz-Gil J., Ugas L., Blesa R., Reñé R., & Costa A. (2017). Language deterioration in bilingual Alzheimer's disease patients: a longitudinal study. *Journal of Neurolinguistics*, 43, 59-75.

Ruiz de Miras J., Costumero V., Belloch V., Escudero J., Ávila C., & Sepulcre J. (2017). Complexity analysis of cortical surface detects changes in future Alzheimer's disease converters. *Human Brain Mapping*, 38, 5905-5918.

Costumero V., Marín Marín L., Calabria M., Belloch V., Escudero J., Baquero M., Hernandez M., Ruiz de Miras J., Costa A., Parcet M.A., & Ávila C. (Submitted) A cross-sectional and longitudinal study on the protective effect of bilingualism against dementia using brain atrophy and cognitive measures.