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# Hippocampal adaptations in Mild Cognitive Impairment patients are modulated by bilingual language experiences

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## Abstract

Bilingualism has been shown to contribute to increased resilience against cognitive aging. One of the key brain structures linked to memory and dementia symptom onset, the hippocampus, has been observed to adapt in response to bilingual experience – at least in healthy individuals. However, in the context of neurodegenerative pathology, it is yet unclear what role previous bilingual experience might have in terms of sustaining integrity of this structure or related behavioral correlates. The present study adds to the limited cohort of research on the effects of bilingualism on neurocognitive outcomes in Mild Cognitive Impairment (MCI) using structural brain data. We investigate whether bilingual language experience (operationalized as language entropy) results in graded neurocognitive adaptations within a cohort of bilinguals diagnosed with MCI. Results reveal a non-linear effect of bilingual language entropy on hippocampal volume, although they do not predict episodic memory performance, nor age of MCI diagnosis.

## Introduction

Managing more than one language in the brain involves a set of cognitively demanding tasks. As competing language representations are always active, irrespective of context, need or conscious intent of use, ensuing mental conflict must be resolved (Kroll & Bialystok, 2013; Marian & Spivey, 2003). On the surface, doing so appears to be effortless, but it is well documented that the mental exercise of dual language control places increased demands on domain general attention and cognitive control resources (Bialystok & Craik, 2022; Green, 1998). Neurocognitive adaptations can stem from the cumulative effect of the added cognitive load (Green & Abutalebi, 2013). They are observed at all stages of life, but especially so in children and older adults where one's cognition is not (yet or any longer, respectively) at its peak (Bialystok, 2017; Bialystok et al., 2004). Bilingualism is increasingly recognized as a significant contributor to reserve and resilience against neurocognitive aging (see Gallo et al., 2022 for review). In this sense, bilingualism is not so different from other lifestyle factors such as higher levels of education, sustained physical exercise, and occupational attainment (Clare et al., 2017; Foubert-Samier et al., 2012). Resilience is commonly operationalized under definitions of COGNITIVE RESERVE and BRAIN RESERVE. These refer to proposed mechanisms that interact with neurocognitive trajectories of healthy and clinical aging (Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia, 2022). Cognitive reserve is a theoretical construct that infers the existence of compensatory processes in the brain, accounting for observable dissociation between better-than-expected cognitive status given the degree of age- or disease-related brain changes (e.g., degree of neural atrophy or clinical pathology (Stern, 2002; Stern et al., 2020)). Brain reserve is operationalized as one's "neurobiological capital", directly observable as increased gray matter volume/density or white matter integrity. The interaction between the above mechanisms is not yet well understood; however, overarching trends show



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exponents of bilingualism can result in increased resilience and leads to more successful neurocognitive aging (Bialystok, 2021).

The most studied type of dementia in the context of bilingualism is Alzheimer's Disease (AD). In people with AD, it is generally found that bilinguals exhibit evidence of increased cognitive reserve. That is, when matched for cognitive status, bilingual patients tend to show greater neural atrophy in brain areas associated with AD, such as the medial temporal lobe (Mendez, 2019; Schweizer et al., 2012). Supportive findings are shown by Duncan and colleagues (2018), who found bilingual individuals with AD to have more degeneration in the parahippocampal gyri and rhinal sulci (related to memory function), while performing at the same level in episodic memory domain as their monolingual counterparts. Recent evidence for bilingualism-related cognitive reserve also comes from studies taking a novel, inverse approach – namely, Berkes et al. (2021) matched monolingual and bilingual individuals for structural brain health, essentially asking how monolinguals perform cognitively when compared to bilinguals when neural atrophy (and not cognitive performance) is held constant. In this context, monolinguals were much more likely to exhibit symptoms indicating underlying neurodegeneration, suggesting compensation for neural decay in older bilinguals.

The above is supported by a rather consistent observation from cohort studies since the mid-2000s, which have shown a correlation between bilingualism and delays in dementia symptom onset by an average of 4–5 years (Alladi et al., 2013; Bialystok et al., 2007; Craik et al., 2010; Woumans et al., 2015; Zheng et al., 2018). While some cohort studies report null results (Ljungberg et al., 2016) and there is a question as to how any given study can be sure to meaningfully isolate bilingualism from other co-occurring life-style enrichment factors (e.g., Mukadam et al., 2017; Van den Noort et al., 2019), recent meta-analyses are clear (Anderson et al., 2020; Paulavicius et al., 2020). They show that bilingualism is an independent factor correlating to a delayed age of AD symptom onset, although the overall incidence of AD is not reduced in bilinguals (Brini et al., 2020). Given the above observations, it is important to understand more deeply whether (and, if so, how) the bilingual brain deploys accumulated resources when faced with disease. Perhaps a good approach is to examine Mild Cognitive Impairment (MCI) – the precursor to AD (Gauthier et al., 2006) – as the staging ground for potentially salubrious effects of bilingualism. MCI is defined as memory impairment that is more severe than would be expected in normal healthy aging. While patients with MCI do suffer memory issues, unlike AD patients, they retain independence in their everyday life (Kelley & Petersen, 2007; McKhann et al., 2011). Not all MCI patients progress to AD or other types of dementia (Pandya et al., 2016), meaning that MCI is more prevalent than AD. Given the improved state of cognitive functioning relative to AD, as a participant group MCI patients are much more amenable to research of the present type. And yet, bilingual MCI studies are scarce.

While evidence exists showing a correlation between bilingualism and brain adaptations in MCI, findings are variable. Bilingual MCI patients exhibit greater cortical thickness across areas implicated in language and cognitive control than monolingual MCI patients (parts of frontal and temporal lobe, as well as bilateral supramarginal gyri; Duncan et al., 2018). Moreover, Duncan et al. (2018) reported positive correlations between episodic memory recall scores and cortical thickness in the abovementioned regions, suggestive of the language and cognitive control network being implicated in maintenance of memory function, decline of which is the primary symptom of typical AD. Other studies report evidence compatible with an interpretation of cognitive reserve. For example, in a prospective longitudinal study of monolingual and bilingual MCI patients matched for cognitive performance, bilinguals exhibited LESS whole-brain parenchymal volume than monolinguals (Costumero et al., 2020). In the follow-up scan seven months later, monolinguals had lost more parenchymal volume and experienced comparatively more cognitive decline than bilinguals. Another study found that MCI-diagnosed bilinguals and monolinguals did not differ on hippocampal volumes, yet bilinguals performed better on some verbal and non-verbal memory measures (Rosselli et al., 2019). Moreover, bilinguals with MCI have also been shown to simultaneously exhibit decreased and increased regional white matter integrity across different tracts (Marin-Marin et al., 2019). Finally, recent evidence points towards bilingualism contributing to higher resting state functional connectivity in MCI individuals (Marin-Marin et al., 2021), an indication of better functional brain health (Fleck et al., 2017).

To summarize, MCI patients have been reported to exhibit bilingualism-related brain reserve, cognitive reserve, or a combination of both types of reserve across different brain areas. If cognitive reserve and brain reserve are different manifestations of the same general reserve mechanism (Bialystok, 2021; Stern et al., 2019) it is perhaps not surprising that the overview of findings reveals mixed evidence. As expression of reserve shifts from a structural (brain reserve) to a more functional (cognitive reserve) account over time with increasing neurological burden, MCI might indeed be the inflection point that signals the exhaustion of structural reserve and a corresponding shift to functional compensation.

It is worth pointing out that, similarly to findings linking AD symptom onset and bilingualism, MCI onset is reported to be delayed in bilinguals when compared to matched monolinguals (Berkes et al., 2020; Bialystok et al., 2014; Ossher et al., 2013; Ramakrishnan et al., 2017). Higher levels of foreign language instruction during childhood and adolescence have been found to be associated with lower risk of developing MCI in old age (Wilson et al., 2015). However, the delay of symptom onset and diagnosis may be conditional on whether both languages are actively used, as opposed to passive understanding without active engagement (Calabria et al., 2020).

In the present study, we add to the nascent literature by investigating the effects of bilingualism on brain structure and memory performance in a Spanish–Catalan speaking MCI patient population using structural MRI and behavioral testing. In a novel departure from other MCI and bilingualism studies, and in line with recent trends in the larger neurocognition of bilingualism literature (DeLuca et al., 2019; Titone & Tiv, 2022), we do not provide a traditional monolingual-to-bilingual between-group comparison. Instead, we operationalize bilingualism as a continuum in a cohort of bilingual MCI patients, ranging from passive bilinguals who have only comprehension knowledge of Catalan in addition to Spanish, to active bilinguals who use Catalan and Spanish in a balanced manner. Since bilingualism is a spectrum, as is monolingualism, there is no need for a "monolingual control" group (see Rothman et al., (2022), for discussion); instead, it is possible to further examine neurocognitive differences driven by individual-level factors of degree of bilingual engagement itself (de Bruin, 2019; Leivada et al., 2020). Such an approach is also fortuitous in other ways – for example, where a monolingual group is simply precluded by the context. This is in fact the case for our language context: Catalonia.

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While finding a Spanish monolingual group is unproblematic, finding a Catalan one given its sociolinguistic reality would be an insurmountable task.

Following previous findings in healthy aging individuals, where bilingualism suggested a brain reserve in the hippocampus, we focused on this brain structure. The hippocampus has been previously shown to be sensitive to bilingual experiences in young (DeLuca, Rothman, et al., 2020; Mårtensson et al., 2012) and older (Voits et al., 2022) bilinguals, and it is also subject to increased rate of atrophy in aging, when compared to other brain structures (Fjell et al., 2009). It directly supports episodic memory function (O'Shea et al., 2016; Persson et al., 2012), which is one of the first cognitive functions to be impaired in MCI and AD, and hippocampal volume is a key indicator for conversion from healthy cognitive aging to MCI and dementia (Fotuhi et al., 2012). Surprisingly, although the hippocampus is a structure of interest with links to both bilingualism and aging that also carries clinical significance, it has not been directly examined in the context of bilingualism in AD and MCI populations.

In line with previous results in the literature, the present study seeks to address the following research questions:

(1) Does increased engagement with bilingual experiences predict a later onset of MCI symptoms and corresponding MCI diagnosis?
(2) Does bilingual experience predict memory performance in the present cohort of MCI patients?
(3) Is bilingual experience predictive for the degree of structural adaptations in the hippocampus?

For question 1, we expect degree of bilingual experience to predict later age of onset for MCI symptoms. For question 2, in line with results from Duncan et al. (2018), we expect a possible positive association between greater bilingual language experience and episodic memory performance. Regarding question 3, on the basis of the mixed existing evidence from bilingual patients with MCI, one might expect two potential outcomes of bilingualism on hippocampal structure, either: (i) a correlation between increased bilingual experience and greater hippocampal volume, i.e., data which can be interpreted as brain reserve; or, (ii) the hippocampus may show a greater extent of atrophy as a function of increased bilingual experience, when memory performance and cognitive state are both controlled for in the model, in line with the cognitive reserve hypothesis. Given the symptomatic profile and cognitive performance of the present participant pool, to which we turn below, we expect scenario (i) is more likely at their present state of MCI progression.

## Materials and methods

### Subjects

Forty patients with a diagnosis of MCI were recruited for the study with a mean age of 73.75 (SD = 4.27; 12 women). Most patients reported Spanish as their L1 (N = 30); 9 participants spoke L1 Catalan, and one participant spoke L1 Galician. Knowledge of languages other than Spanish, Catalan or Galician was not reported. Subjects reported a variable age of MCI symptom onset (range 58–84) (based on a report of the relatives or according to the clinical history) and formal MCI diagnosis (59–84) (for an overview of study sample demographics, see Table 1).

The participants in this sample scored relatively high in the Mini-mental state examination (MMSE), a screening test where the cut-off score of 24 is typically used for differentiating patients with suspected MCI or mild AD (range: 25–30) (Arevalo-Rodriguez et al., 2021). MMSE alone is sensitive to moderate cognitive decline (multiple domains of cognition with an impact on everyday life), typically found in the early stages of dementia (Diniz et al., 2007), but the sensitivity and specificity of the MMSE alone to detect MCI is very low (73%), with a cut-off score of 28 out of 30 (Ciesielska et al., 2016). Therefore, in addition to MMSE, we used standard methods for the diagnosis of MCI in our patients that are used in many countries across the world. The MCI diagnosis was done by neurologists and clinical neuropsychologists at the hospital according to the recommendations from the National Institute on Aging Alzheimer's Association (Albert et al., 2011), meeting the following criteria: a) subjective or informant-based cognitive decline; b) objective deficits of one or more cognitive domains, typically including memory from the neuropsychological assessment; c) the cognitive decline is not interfering with individual independence; d) Clinical Dementia Rating score = 0 suggesting absence of dementia; and e) onset after the age of 65 (usually in the late 70s or thereafter). The presence of cognitive impairment (point b) was based on an extensive neuropsychological assessment that included tests for verbal and non-verbal long-term memory, short-term and working memory, visuospatial and visuoconstructive abilities, attention, executive control functions, verbal fluency, and naming. Additionally, for this study we collected neuropsychological scores from: the CERAD Word List Memory (Morris et al., 1989), which measures long-term episodic verbal memory; the forward and backward Digit Span tasks (Spanish normative data: Peña-Casanova et al., 2009), which measure verbal short-term memory; and the Trail Making Test part A (Spanish normative data: Peña-Casanova et al., 2009), which measures visual attention and motor speed.

All subjects resided in Spain, were self-reported highly proficient users of Spanish, with early exposure to Spanish (most at birth, a few at ages 4–6) and high fluency in this language. Unlike Spanish, reported exposure, engagement, and fluency in Catalan was varied, but all individuals had at least a passive understanding of Catalan. The data were collected from the Bellvitge University Hospital, L'Hospitalet de Llobregat (Spain).

**Table 1.** Overall demographics and language background of the MCI patient sample (n=40; 12 F/ 28 M)

| | Mean | SD | Range |
|---|---|---|---|
| **Age** | 73.75 | 4.27 | 63-84 |
| **Years of education** | 7.82 | 4.11 | 0-20 |
| **Cognitive Reserve Index** | 94.35 | 18.87 | 69-138 |
| **Age at MCI symptom onset** | 69.58 | 5.15 | 58-84 |
| **Age at MCI diagnosis** | 72.53 | 4.94 | 59-84 |
| **MMSE** | 27.2 | 1.34 | 25-30 |
| **Age at Spanish exposure (years)** | 0.58 | 1.57 | 0-6 |
| **Age at Catalan exposure (years)** | 14.93 | 10.9 | 0-35 |
| **Self-reported Catalan proficiency (out of 20)** | 13.9 | 4.99 | 6-20 |
| **Self-reported Spanish proficiency (out of 20)** | 19.42 | 0.78 | 17-20 |
| **Language entropy** | 0.48 | 0.43 | 0-1 |

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### Language background and demographic measures

Detailed language and demographic information data were collected. Language history was assessed using a questionnaire administered to the participants and an interview with the patient and relatives (see Calabria et al., 2021). The data collected included the following measures: Age of acquisition of each language (Catalan and Spanish), self-reported language proficiency, and language use frequency.

Self-reported language proficiency was assessed on a four-point Likert scale (1 = poor, 2 = regular, 3 = good, 4 = perfect) based on five domains (speaking, comprehension, writing, reading, and fluency). Scores across all five domains were summed to obtain a total proficiency score. Language use was assessed in terms of the percentage of time spent in either a Spanish- or Catalan-dominant environment across the lifespan, where a score of 0 means a Spanish-only environment, 100 means Catalan-only and 50 denotes a perfectly balanced exposure. This metric was used to calculate a language entropy measure using the languageEntropy R package (Gullifer & Titone, 2018). Language entropy is a measure that characterizes the diversity of language use. In a bilingual context, language entropy ranges from 0 to 1. In the present sample, 0 denotes an entirely single language use across the lifespan, whereas 1 denotes a perfectly balanced engagement with both languages (for language background information see Table 1). Language entropy has been shown to generalize well to multilingual contexts and relates to various cognitive and neural processes (Gullifer et al., 2018; Gullifer & Titone, 2020).

In addition to the MMSE (Folstein et al., 1975), participants also completed the Cognitive Reserve Index questionnaire (CRIq), a tool that allows for the estimation and quantification of cognitive reserve – by taking into account education, work, and leisure activities (Nucci et al., 2012). Notably, the CRIq does not account for bilingualism.

### Memory tasks

The behavioral testing battery included an episodic memory task, based on the recognition memory paradigm (old/new) (for details, see Calabria et al., 2020). In short, participants were shown 30 grayscale photos of unfamiliar faces and asked to rate whether they found them attractive or not. Participants were also asked to try and remember the faces. This was followed by a delayed surprise recognition task where previously seen faces were presented alongside 30 novel faces and participants had to indicate whether the stimulus was presented in the encoding phase, or not. Performance was measured as d′ scores (d′ = ZHit – ZFA, where ZHit and ZFA are z transforms of hit rate and false alarm, respectively).

In addition to the visual recognition task, participants completed the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word List Memory task, measuring verbal episodic memory (Morris et al., 1989). This is a test including a free recall and recognition measure that is sensitive to dementia. The participants were presented a word list of 10 words over 3 trials with scrambled presentation order in each trial. The participants then had to recall as many words as they could.

### MRI acquisition protocol and preprocessing pipeline

Participants underwent structural MRI scanning. High resolution T1 anatomical scans were acquired using a 3T MRI scanner (Discovery MR750w, GE Healthcare Systems, Milwaukee, Wisconsin) using a 32-channel head coil (196 sagittal slices, 1 mm slice thickness, TR = 9.532 ms, TE = 3.716 ms, flip angle = 12°, matrix 256 × 256, voxel size 1 mm isotropic). The volumetric MRI analyses, i.e., hippocampal volumetric segmentation, were based in the FreeSurfer 6.0.0 image analysis suite (http://surfer.nmr.mgh.harvard.edu/). We ran the standard recon-all pipeline, which removes non-brain tissue using a hybrid watershed/surface deformation procedure (Ségonne et al., 2004), performs automated Talairach transformation, segmentation of deep gray matter volumetric structures (including the hippocampus; Fischl et al., 2002, 2004), intensity normalization (Sled et al., 1998), tessellation of the gray matter white matter boundary, automated topology correction (Fischl et al., 2001; Segonne et al., 2007). Freesurfer morphometric procedures have been demonstrated to show good test-retest reliability across scanner manufacturers and across field strengths (Han et al., 2006; Reuter et al., 2012).

After completion of the recon-all pipeline, we extracted the left and right hippocampal volumes for each individual, which were summed to obtain total hippocampal volume. This value was then divided by the individual estimated total intracranial volume to provide normalized values for further statistical analyses.

### Statistical modeling

Demographic, behavioral, and structural MRI data were analyzed in R 4.1.2. (R Core Team, 2021) with generalized additive models (GAMs), by using the gam() function of the mgcv package (Wood, 2017). GAMs were selected as a method that can account for potential nonlinear effects of bilingual experience on the onset and progression of neurocognitive decline. This is important as the pattern of effects of bilingualism in healthy and clinical aging populations is not well understood and it may follow a nonlinear pattern. Specifically, GAMs fit a nonlinear regression spline consisting of the sum of simpler smooth patterns that can be linear or nonlinear. GAMs report the nonlinearity of the effect in the form of estimated degrees of freedom (edf), where edf = 1 denotes a linear term, and edf>1 indicates a nonlinear term. Separate GAMs were run for volumetric analyses, behavioral (episodic memory) analyses, and age of MCI symptom onset/diagnosis. This was done in a stepwise manner – base models included covariates of no interest (see individual descriptions for each dependent variable set below), while an expanded model added language entropy score to the model structure as the main predictor. This was done to see if an effect of bilingualism can be captured over and above other covariates that may affect neurocognitive outcomes.

Throughout our models we chose to employ language entropy as a proxy for bilingual experience which quantifies time spent in a dominant context for each language throughout one's lifetime, thus making it the most nuanced way to approach the variable of actual exposure/engagement. It also highly correlated with self-reported Catalan proficiency ($R = 0.91$, $t(38) = 13.24$, $p < 0.001$), which was a much less detailed predictor, being only an aggregate of multiple Likert-scale self-reported score measures ranging from 1 to 4. In addition, proficiency measures in general are different from the engagement score: as they do not capture the bilingual experience in the same way engagement with one's languages can (DeLuca et al., 2018). Considering the combination of the above reasons, the proficiency measure was disfavored. Spanish proficiency could not be included as a predictor as all participants self-rated their Spanish proficiency at near-ceiling and thus there was little variability in this predictor. As CRIq scores significantly

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correlated with language entropy ($R = 0.54$, $t(38) = 3.98$, $p < 0.001$), CRIq was not included as a predictor to avoid multicollinearity. For all models run, we also tested a version with CRIq as a predictor in interest. In all cases, introduction of this variable increased the concurvity in the models. This is expected, as collinearity in the dataset typically introduced a greater concurvity between independent variables in GAMs. See Appendix A for correlation matrix of the variables of interest.

### Volumetric analysis

We built and implemented GAMs to estimate the effects of bilingualism on normalized total hippocampal volume, which was used as the dependent variable in this set of analyses. The first-level model included a regression spline of age, along with random effects of sex and participant. The second-level model added behavioral metrics – MMSE score and memory performance – as a main effect. Finally, the third-level model added a regression spline of language entropy.

### MCI symptom onset and age at diagnosis, MMSE scores

The second set of analyses tested the effects of bilingual experience on the age at MCI symptom onset and age of MCI diagnosis. Here, we ran a model with a regression spline of language entropy as a predictor along with random effects of sex and participant. This process was repeated with age at MCI diagnosis as the predicted value. Additionally, we tested the effects of bilingualism on MMSE scores at the time of testing, including a regression spline of age, random effects of sex and participant in the base model and adding language entropy to the second-level GAM.

### Behavioral analysis

We also carried out an analysis to estimate episodic memory performance as a function of language entropy. As participants had completed two tasks tapping in the same cognitive domain (episodic memory), we performed an unrotated Principal Components Analysis on the face recognition task d′ scores and CERAD word recall scores, to reduce the number of variables in the regression and create a summary score variable capturing episodic memory performance. This component captured an approximately equal amount of variance from both individual episodic memory measures (53.9% CERAD; 46.1% Face recognition) and was used as the dependent variable in this set of models. Then, we ran a set of GAMs in a stepwise manner of increasing complexity. In the first-level model, we fit a regression spline of age, along with random effects of sex and participant. Then, as step 2, a regression spline of MMSE and hippocampal volume (to control for the variability in neuroanatomy) was added to the model. Finally, the model was expanded by adding language entropy as a main predictor in step 3.

## Results

### Volumetric analysis of the hippocampus

The base model revealed no significant effects of any predictor, although the effect of age was trending at $p = 0.09$. The second-level model revealed no significant predictors of hippocampal volume. However, the final model revealed both age and language entropy as significant predictors. This most complex model was the best fit (AIC = -476.6804, compared to -471.6974 and -470.1728 respectively). Age was non-linearly correlated to total hippocampal volume ($p = 0.0318$, $edf = 1.743$), whereas language entropy showed a non-linear inverted U-shaped association with hippocampal volume ($p = 0.0292$; $edf = 2.616$), such that hippocampal volume was the largest with mid-ranged language entropy scores – that is, where there is significant, but not balanced, usage of the two languages (See Fig 1.).

### Analysis of age of MCI symptom onset, age at formal MCI diagnosis, and MMSE scores

None of the variables across models predicted age of MCI symptom onset nor age at formal diagnosis. Additionally, the most complex model with MMSE score as the dependent variable revealed a significant linear effect of language entropy ($p < 0.01$; $edf = 1$), and a non-linear effect of total hippocampal volume ($p = 0.042$; $edf = 3.75$) (Fig. 2) as well as random effects of sex ($p < 0.01$; $edf = 0.92$) and participant ($p < 0.01$; $edf = 0.88$).

### Behavioral results: Episodic memory

Episodic memory performance was significantly predicted by random effects of participant ($p = 0.049$; $edf = 7.69$) – however, no other variables, including language entropy, emerged as significant predictors for episodic memory.

## Discussion

In line with current theoretical models and discussions in the literature, we turn our efforts to unpack and interpret our findings. The present study aimed to answer three questions: (1) does increased engagement with bilingualism predict a later age of onset of MCI symptoms and a corresponding MCI diagnosis; (2) does bilingual experience predict memory performance in the present cohort of MCI patients; and (3) is bilingual experience predictive of volumetric adaptations in the hippocampus and/or (related) cognitive task performance? While our findings are null with respect to questions 1 and 2 (although language entropy significantly predicted MMSE scores), a non-linear relationship between bilingual experience and hippocampal volume (question 3) was found, but no evidence was found for an impact on cognitive task performance. Given the results are most illustrative for the third question posed, some special attention seems appropriate before further unpacking the data in line with all questions in the sequence they were presented. Recall that we anticipated two potential scenarios for question 3: (i) evidence for brain reserve in terms of bilingual engagement volumetric correlations or (ii) in the absence of such evidence, a potential for bilingual engagement to correlate with evidence for cognitive reserve in task performance. We already anticipated expecting (i) as more likely for our pool of participants given their relatively high MMSE scores. The underlying logic was that our pool is mostly populated by individuals at an early stage of MCI, a point at which we would still expect evidence of brain reserve (the accrued tissue would not yet be depleted). Adding to this, the fact that everyone did well on the cognitive tasks – that we see a lack of overt relationship (a null effect seemingly relevant for research question 2) between on-task episodic memory performance as predicted by bilingual experience – could be because progression of MCI in our cohort is not (yet) past a threshold where cognitive reserve effects would kick in. To the extent that brain reserve and cognitive reserve are related, in the sense that the latter is subsumed under the former and thus likely to be observed after the accrued

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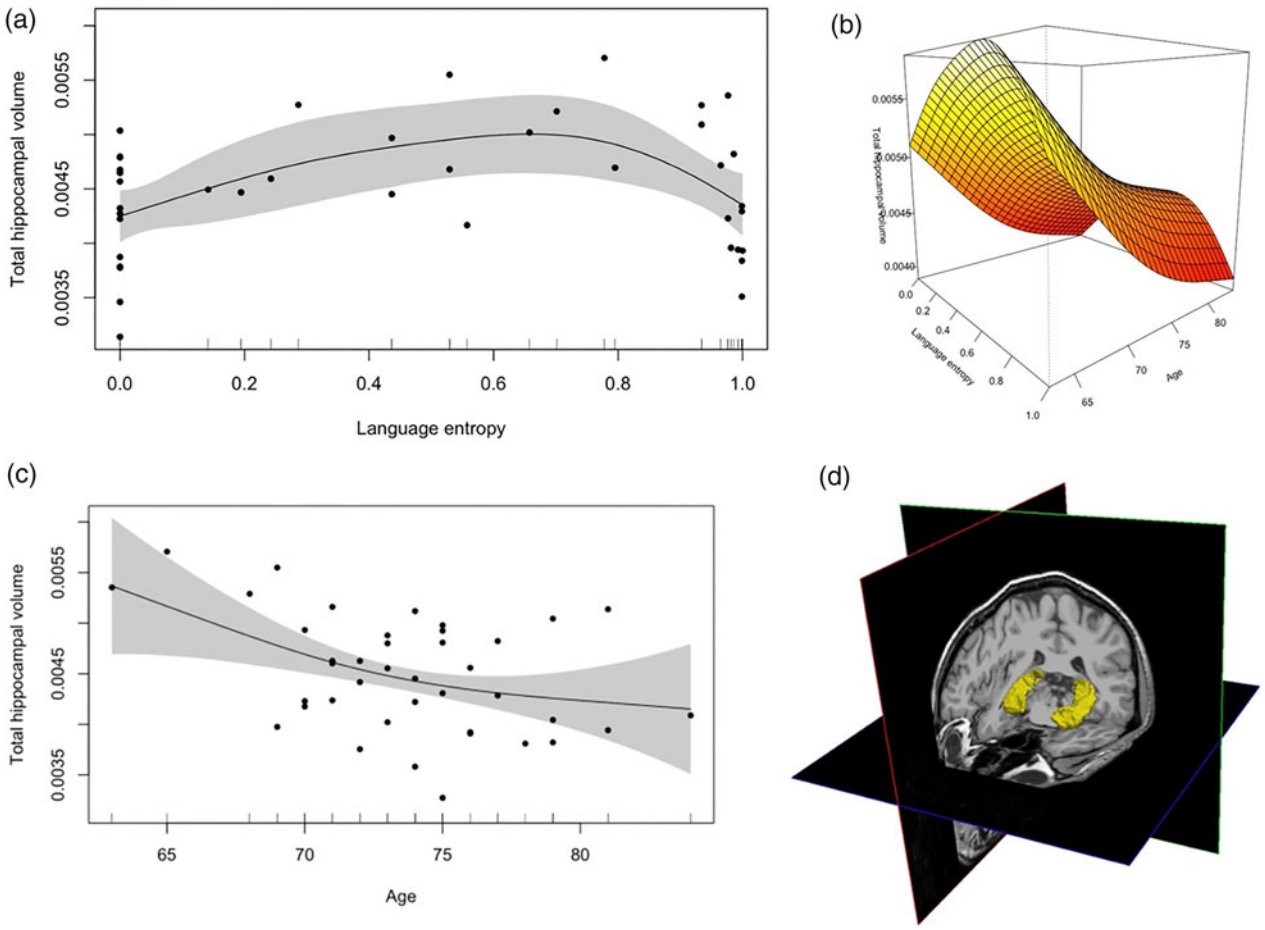


**Figure 1.** Partial effect plots of age and language entropy on normalized total hippocampal volume (panels A and C, respectively). Panel B shows a 3d visualization of the relationship between these variables. On panel D, a visualization of the hippocampal template used as the basis for the Freesurfer segmentation pipeline. Image generated using freeview image viewer, Freesurfer software package.

neuronal tissue is depleted (Berkes et al., 2021; Voits et al., 2020), then it makes sense that (ii) would necessarily be descriptive of MCI patients at later stages of progression. And so, while (i) describes the current participant pool it does not preclude (ii) from being shown in a different set of subjects. In fact, in a longitudinal approach, were we able to follow these same subjects, we might expect a shift where (ii) is evidenced.

The absence of a relationship between bilingualism and age of MCI symptom onset or age at MCI diagnosis in our population is perhaps a little surprising, not least since a significant number of studies report similar effects (see e.g., Anderson et al., 2020 for review). It is prudent to keep in mind that most previous studies did not regress degree of bilingual engagement as we did here. Rather, often with much larger samples, they show a generalized bilingualism-to-monolingualism group comparison where bilingualism as a group variable is associated with a protracted age of onset of symptoms/diagnosis. Studies on aging that treat bilingualism as a continuum are rare. Even so, some have found the

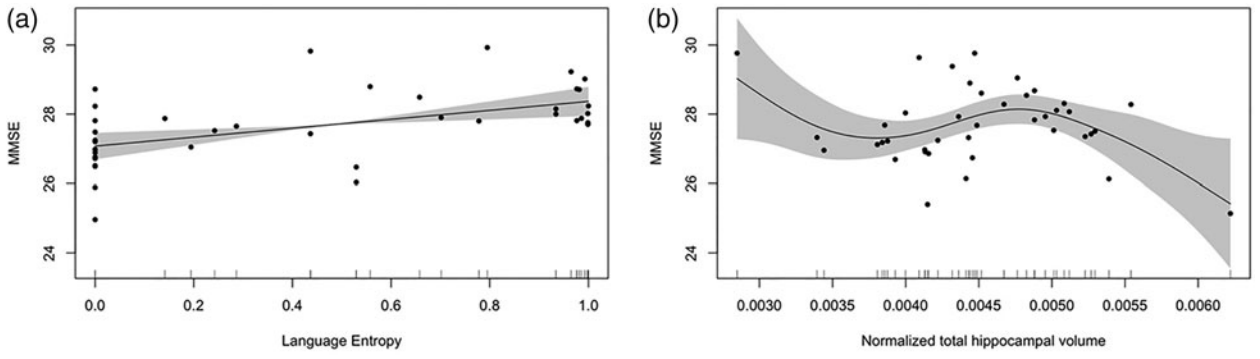


**Figure 2.** Partial effect plots of language entropy (panel A) and hippocampal volume (panel B) on MMSE scores at the time of testing.

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correlation between bilingual experiences and age of MCI symptom onset (e.g., Calabria et al., 2020 where the participant sample is from the same context). However, the participant population in Calabria et al., 2020 (n = 135) was significantly larger (and the reported delay was smaller than the 4–5 years reported in other studies – e.g., Alladi et al., 2013): so the lack of observed effect in our sample could be a byproduct of reduced statistical power. Although language entropy was not predictive of memory performance in the present context, correlations were observed between it and MMSE scores. Indeed, greater language entropy predicted MMSE scores in the expected direction (i.e., positive association between these variables).

The data suggestive of effects of bilingual engagement on hippocampal volume are perhaps the most interesting ones. As bilingualism has been linked to structural adaptations in the hippocampus in immersed younger populations (DeLuca et al., 2019; Mårtensson et al., 2012), as well as healthy older adults (Voits et al., 2022), the finding of hippocampal volumetric sensitivity to bilingualism in an MCI-diagnosed sample is not surprising *per se*. What is more intriguing, perhaps at first glance perplexing, is the inverse-U shaped curve with respect to degree of bilingual language entropy.

The inverse-U shaped curve indicates that degree of bilingual language engagement matters for hippocampal volumetric adaptations with MCI, in line with related contemporary discussions with non-clinical populations (e.g., DeLuca et al., 2019; Gullifer & Titone, 2020; Luk & Bialystok, 2013; Titone & Tiv, 2022). The highest hippocampal volumes were observed for individuals with mid-range levels of bilingual engagement, while both functional monolinguals and individuals with the most balance in terms of dual usage patterns (entropy scores approaching 1) exhibited comparatively smaller hippocampal volumes. At first consideration, then, such a pattern might seem either counter-intuitive and/or a basis for questioning the relationship between hippocampal volume and reserve accrual from bilingual language engagement in the first place. We submit, however, that such a pattern is perfectly predicted by recent theoretical models that explain such U-shape patterns in terms of neuroplastic efficiency (DeLuca, Segaert, et al., 2020; Pliatsikas, 2020).

In short, under this more nuanced approach, the working hypothesis is precisely that low-to-medium engagement would yield volumetric distinctions because up to this point bilingual processing is cognitively most taxing. Under such an interpretation, morphological brain changes of the sort observed with medium level of engagement are: (a) a result of the cognitive demands implicit to increased engagement to a particular ceiling threshold; and (b) an intermediary stage on a continuum of potential maximal engagement that eventually privileges efficiency. In other words, past a particular quantity of bilingual language engagement – on the higher end of the spectrum – a return to baseline in the brain is expected given that the heightened degree of bilingual engagement lends itself to automatization of what engagement proxies for (e.g., regulation of attentional control, inhibition; for recent findings dynamic neural adaptations in cognitive control regions, see Korenar et al., 2021; Marin-Marin et al., 2022). Hippocampal adaptations fit well in this framework, too, as novel word learning is facilitated by processes in the hippocampus (Berens et al., 2018): therefore, adaptations in the initial stages of second language acquisition or with low engagement with one's second language are theoretically warranted, followed by subsequent structural reductions as the need to learn/encode new linguistic items dissipates with increased language experience. The back-to-baseline effects themselves are understood as signs of increased neural efficiency, which no longer needs increased neuronal resources. Thus, the U-shaped curve we see is itself a reflection of the trajectory that individuals at the highest level of balanced bilingual engagement would have passed through. Cumulatively speaking, such individuals would, in principle, have passed through an intermediary stage over their lifetime of experience where their hippocampus would have been comparatively larger in volume, but after a certain critical mass of engagement their hippocampus returned to baseline because they became increasingly more efficient at dealing with the implicated cognitive demands. Thus, bigger is not necessarily (always) better – precisely because the larger something is, the more energy/resources it consumes.

Relating the above discussion to the theoretical landscape, the pattern we observe is predicted by (and, thus, supportive of) the Dynamic Restructuring Model (DRM) (Pliatsikas, 2020). The DRM is an account that explains variability of brain adaptations in response to bilingual language experiences based on length/intensity of bilingual experience and the plasticity properties of the brain – adaptations to increased demands when acquiring new skills, followed by pruning of any structural excess (i.e., return to baseline) when a skill is learned and consolidated. In the initial stages of second language acquisition the DRM predicts volumetric increases across cortical and subcortical gray matter to accommodate for increased processing load that the brain must cope with. In the following phase – consolidation – one would observe increases in white matter structural integrity and renormalization of cortical gray matter. Finally, as the bilingual individual reaches 'peak efficiency', the DRM expects continued return to the volumetric baseline of the gray matter structures and strengthening of white matter tracts.

Extending this approach to the present data, we submit that the general tenets of the DRM apply whereby the level of engagement/language entropy is ultimately what determines the stage at which an individual finds oneself (perhaps remains indefinitely) at any point in time rather than purely the linguistic stage of acquisition itself (i.e., age of second language acquisition). Using this DRM-inspired approach, our data bear out: hippocampal volume is predicted to be the greatest in those who are not balanced in their bilingual language use patterns (i.e., are not (yet) at 'peak efficiency') – as opposed to both those who have only a passive understanding of their additional language and those who are more balanced in their bilingual engagement patterns. Thus, more effortful processing, associated with unbalanced and cognitively more taxing language use, could be the driving force behind providing a structural reserve for the hippocampus. As the hippocampus is shown to be sensitive to aging (Fjell et al., 2009), and it plays a key role in development of AD (Fox & Schott, 2004), evidence for reserve in this region suggests potential increased neuroprotective effect of bilingualism, which may be the underlying mechanism of the previously reported delayed progression to AD.

The present study, just like other studies of this type, is not without its limitations. Specifically, if one considers the level of engagement or language entropy to be a core predictor for neurocognitive adaptations, it is not and cannot be constant over time. Patterns of linguistic engagement and use are subject to change over one's lifespan. Yet data collected in a cross-sectional design are merely a snapshot in time and cannot account for temporal variation, thus warranting future longitudinal research. Furthermore, one could wish for a greater granularity in the

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linguistic (and other) data, but there are practical constraints when working with clinical populations – one is often limited to the type of information one has access to. And so herein we relied on reports of current language use patterns as the core predictor for neurocognitive adaptations – however, future research should aim to collect data allowing for examination of these relationships in a more granular manner.

## Conclusion

This study contributes to the nascent literature examining potential neurological effects of bilingualism in clinical aging. We tested our predictions with generalized additive modeling, allowing us to capture nonlinear relations between variables of interest. Bilingual engagement emerged as a significant predictor for total hippocampal volume: but we found no effects of bilingualism on the age at MCI symptom onset, age at MCI diagnosis, nor episodic memory performance.

With an increasingly aging population and no current pharmacological cure for progressive neurodegeneration, such as MCI or AD, it is imperative to explore alternatives that may provide for healthier and longer quality of life. It has been argued that bilingualism can be viewed as a 'solution hiding in plain sight' for this impeding public health crisis (Bialystok et al., 2016); still, it is crucial to understand the exact effects of bilingualism on brain and cognition and the mechanisms that afford the delays in symptom onset and diagnosis moving forward. In light of the present results, the cognitive exercise associated with bilingual engagement can be considered as a contributor to neural resilience, at least when it comes to adaptations commensurate with structural reserve in one of the key brain structures associated with dementia.

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**Competing interests.** The author(s) declare none.

**Data availability.** The data that support the findings of this study are openly available in Open Science Foundation at http://doi.org/10.17605/OSF.IO/SBPE2.

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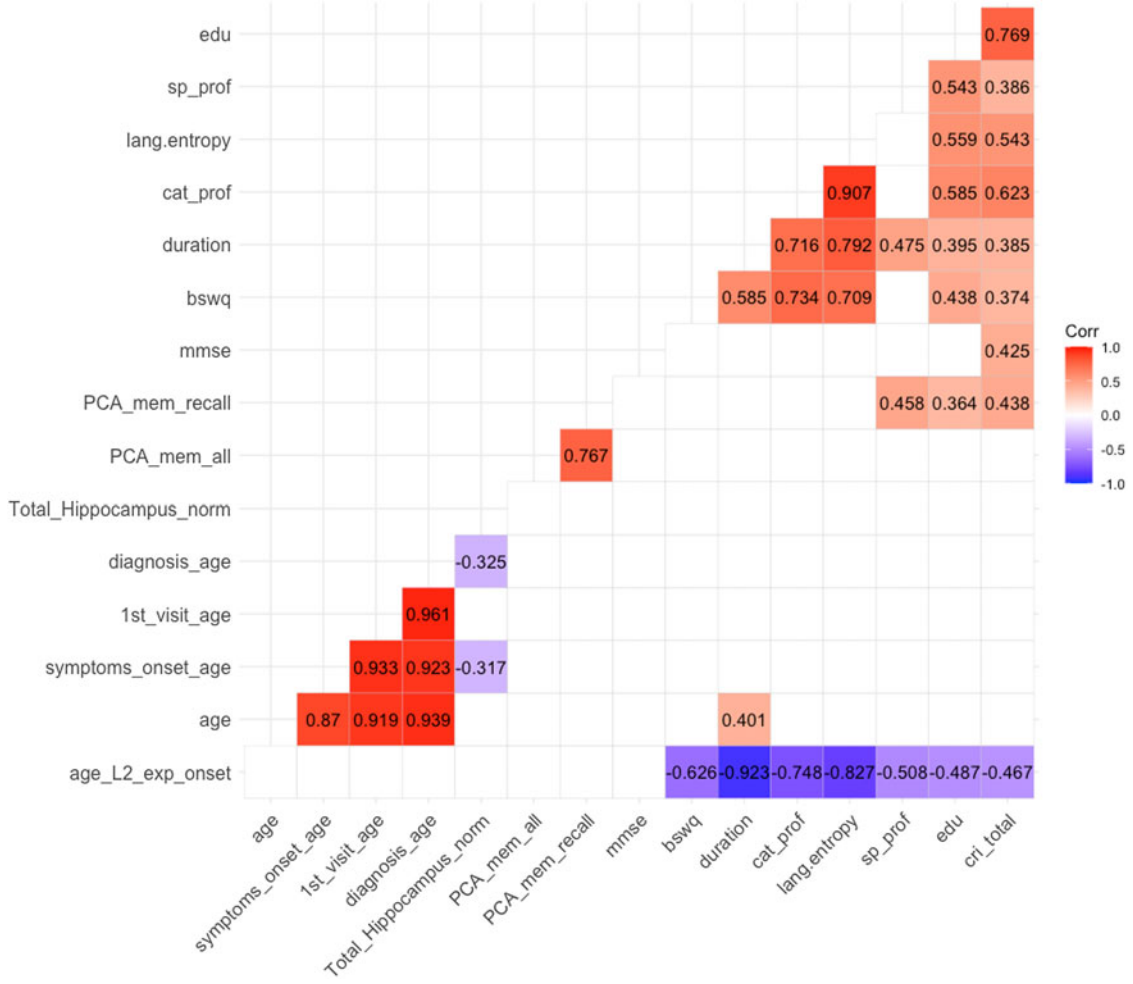
## Appendix A.




**Appendix A.** Correlation matrix of the variables of interest. Only significant pairwise correlations are reported in the matrix.

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