

# Comparing the impact of lifelong multilingualism and later-life language learning on cognitive and brain reserve in older adults with cognitive decline due to Alzheimer's disease: A systematic review

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**Abstract.** The neurocognitive adaptations associated with language engagement have received particular attention in research on dementia prevention. Studies suggest that by placing great demands on executive functions, (lifelong) multilingualism (LM; juggling two or more languages in daily life through lived multilingual experience) and later-life language learning (LLLL; starting new language learning in older adulthood through language training, where previously only one language was used in everyday life) cause changes in the neural substrate, enhancing reserve and sustaining cognitive functioning (Antoniou and Wright 2017; Bialystok 2021). However, current research has not yet directly investigated the ways and degree to which LM and LLLL differ in their impact on neurocognition. This systematic review addresses this gap by comparing the scope of LM and LLLL impact on cognition in older adults across different stages of Alzheimer's disease, alongside examining the effect of LM on brain structure and function. A systematic search was conducted on PubMed, Web of Science, Scopus, and PsycINFO. Eighteen empirical studies, comprising sixteen on LM and two on LLLL, were included and reviewed in connection with current theoretical models on the role of bilingualism as a reserve-enhancing factor. Findings show that LM contributes to the development of brain and cognitive reserve by engaging cognitive control and inducing neurocognitive adaptations from early to severe stages of Alzheimer's disease, while protective effects of LLLL were mainly observed on memory. Nevertheless, a general lack of studies and variability in study design and terminology highlighted the need for further research.

**Keywords.** multilingualism, later-life language learning, cognitive reserve, brain reserve, Alzheimer's disease

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## 1 Introduction

Although, as a general trend, the world's population is aging, longevity does not necessarily presuppose the preservation of good physical and mental health. In particular, with the global increase in dementia incidence and the absence of a disease-modifying pharmacological cure, the development of prevention strategies directed at delaying or containing the emergence of age-related and disease-related cognitive decline through non-pharmacological interventions has been and continues to be a primary aim of the World Health Organization's global agenda (World Health Organization 2021). The idea that symptoms of cognitive decline might be delayed or prevented derives from findings on inter-individual variability in the manifestation of cognitive deficits. With specific regard to Alzheimer's disease (AD), which represents the main cause of dementia (World Health Organization 2023), prospective studies have found that between 10% and 40% of people, diagnosed with AD at autopsy, had shown no signs of cognitive impairment prior to death (Mortimer 1997).

To explain these findings and, more broadly, diverging patterns of cognitive decline, the concepts of Cognitive Reserve (CR) and Brain Reserve (BR) have been posited. Although the terms are not without problems (Kremen et al. 2022), BR is generally taken to denote individual structural neural differences in the capacity to sustain brain damage. Larger brain sizes tend to tolerate a higher degree of atrophy before cognitive deficits become clinically and behaviorally evident, because cognitive functioning can rely on remaining neural structures (Stern 2009). Depending on the BR of an individual, the threshold where cognitive deficit symptoms do become overtly noticeable might be reached at different levels of disease severity (Stern 2002). In contrast, CR builds on the premise that the brain actively counters damage by engaging existing neural networks in various ways, independently of BR. This may manifest in a more efficient use of neural networks, either through increased activation or the individuation of a greater array of different neural networks to perform a specific task (*neural reserve*), or the recruitment of alternate neural networks that would not usually be involved in the execution of a specific cognitive task in case of brain damage (*neural compensation*) (Barulli and Stern 2013). As is the case for BR, however, individual differences exist in CR, which differentially modulate the clinical expression of neuropathology. Additionally, although Stern's original definition of BR and CR treated both as separate constructs, their interaction has recently been challenged (Coors et al. 2024).

Research suggests that the placement of higher demands on the individual through rich and stimulating environments and lifestyles might provide a form of "training" for the brain, contributing to BR and CR and thus leading to individual differences in cognitive performance (Antoniou, Gunasekera, and Wong 2013). More specifically, several activities or life experiences can foster reserve in an individual, and thus be considered as "cognitively stimulating" (Katzman 1995). Higher levels of educational attainment, for instance, have been reported to build reserve by generating long-term neural potentiation (Addae, Youssef, and Stone 2003). Additionally, since cognitively stimulating activities are also crucial for reserve maintenance, they have been recently implemented in dementia prevention programs directed at older adults, with the goal of maintaining cognitive health (Orrell and Sahakian 1995). Cognitive interventions might involve learning to play a musical instrument, solving crosswords, and learning a new language (Klimova, Valis, and Kuca 2017). From this perspective, the study of language engagement as a cognitively stimulating life experience is particularly relevant. Specifically, two instances of language engagement have been examined in the literature in relation to reserve enhancement, namely (lifelong) multilingualism (LM), used in this paper as an umbrella term to indicate the sustained use of more than one language throughout life in various contexts, usually independent of formal education and proficiency level (Pot, Keijzer, and Bot 2018; Gallo and Abutalebi 2024) and later-life language learning (LLLL), which denotes the experience of learning a new language in later-life, either in healthy or cognitively impaired older adults, as part of an intervention to sustain or improve cognitive performance (Keijzer et al. 2023).

Recent studies have indicated that both LM<sup>2</sup> and LLLL might protect against the emergence of cognitive decline in older adulthood due to their contribution to BR and CR. Numerous empirical studies have highlighted that bilingualism is associated with delays in dementia onset, as well as better performance on cognitive tests, with bilinguals either displaying a higher degree of pathology than monolingual peers with similar levels of cognitive performance or, contrarily, outperforming them at a comparable level of neuropathology (Bialystok 2021; Gallo and Abutalebi 2024). Such a "bilingual advantage" has been explained as the constant activation of competing languages placing heavier demands on cognitive resources related to language and executive control, thus leading bilinguals to rely more on the attentional control mechanism, which is enhanced by becoming more efficient, flexible, and powerful, both in maintaining current goals and resolving conflicts. In other words, by engaging cognitive operations such as interference suppression, response inhibition, and goal maintenance, that are part of and supervised by attentional control, bilingual language processing might strengthen this mechanism, which, in turn, sustains various cognitive abilities, such as cognitive flexibility and conflict resolution (Bialystok and Craik 2022). Therefore, speaking multiple languages might increase CR through the enhancement non-verbal domain-general cognition. Similarly, the demands imposed by learning and speaking multiple languages appear to drive structural and functional brain changes, with a general optimization of neural networks involved in language and executive control in response to higher demands being placed on such mechanisms, and further adaptations depending on individual bilingual experiences, suggesting a potential pathway for BR development (Pliatsikas 2020).

2. This term will be preferred over *bilingualism* to encompass a wider range of language use patterns; however, the term *bilingualism* will be maintained when reporting studies using this term.

In the realm of LLLL, evidence suggests that the aging brain still retains some degree of neuroplasticity and, together with the observed correspondence between the neural network exploited by language learning and that decaying due to aging, led to the idea that learning a language in older adulthood might promote or maintain healthy cognitive functioning in aging and ultimately delay the emergence of cognitive decline (Antoniou and Wright 2017; Antoniou, Gunasekera, and Wong 2013). However, findings on the role of LLLL as a cognitive intervention are scarce, with only a handful of studies investigating its effects in healthy older adults and a general lack of evidence for older adults on the AD continuum (Keijzer et al. 2023). In fact, the potential of LLLL in dementia prevention is largely based on findings pertaining to LM in the absence of robust evidence from LLLL studies themselves. What is more, albeit promising, the impact of LM on reserve continues to be debated.

Indeed, inconsistent results have been found when investigating LM as a reserve-enhancing factor (Mukadam, Sommerlad, and Livingston 2017), ascribed to differing study designs and, primarily, the heterogeneity of LM experiences (Gallo and Abutalebi 2024). As outlined by de Bruin (2019), the effects of LM on cognition can be modulated by multiple factors that make up the LM experience. Among others, these include age and context of language acquisition, proficiency, language use, code-switching patterns, and contexts of use. Because of that, recent studies have thus largely abandoned the operationalization of LM as a dichotomous variable (multilingual vs. monolingual) that was common practice in earlier work and have instead adopted a multilingual language engagement spectrum (Baum and Titone 2014; Luk and Bialystok 2013). This does more justice to a potential interaction of factors that might regulate the use of cognitive resources and consequently determine the presence—or absence—of neurocognitive adaptations ensuing from multilingualism.

The multilingual language engagement spectrum is often operationalized as different interactional contexts and code-switching behaviors, representing contrasting cognitively stimulating environments. An example of how differing environments shape the demands on cognitive control processes comes from a study by Beatty-Martínez et al. (2019). The study indicated that, at the same level of proficiency, bilinguals who largely move in what they call separated contexts (i. e., the different languages are used in specific, isolated contexts) appear to rely more on reactive control processes like response inhibition, while bilinguals in varied contexts (i. e., where code-switching might be commonplace) seem to recruit proactive control processes, including goal maintenance, conflict monitoring, and interference suppression. On the other hand, bilinguals in integrated contexts (i. e., characterized by dense code-switching) showed lower reliance on control processes, ascribed to opportunistic planning. In a group of healthy older adults, Pot, Keijzer, and Bot (2018) found an association between enhanced cognitive performance and intense usage of multiple languages in environments where context-dependent code-switching was present but could not be resolved through opportunistic planning as in dense code-switching environments (similar to the varied context in Beatty-Martínez et al. 2019). This advantage was attributed to enhanced conflict monitoring, thus corroborating the findings by Beatty-Martínez et al. (2019). Importantly, it appears that it is this specific varied context of multilingual language that translates into the enhancement of domain-general cognitive processes.

The studies discussed above thus suggest that different multilingual language use patterns likely engage different cognitive resources and only specific conditions lead

to domain-general cognitive benefits. Such considerations align with the Adaptive Control Hypothesis (ACH) (Green and Abutalebi 2013), which predicts that the type of interactional context modulates which and to what extent specific control processes are engaged to support the speaker's communicative needs. In particular, a dual-language context where multiple languages are used in the same contexts and code-switching may be required in response to a change in social setting is predicted to induce higher and more complex demands on cognitive control, driving an adaptation in control processes which become more efficient, explaining the earlier experimental results. Furthermore, the ACH predicts adaptive structural and functional brain changes in the control network as a function of interactional language context. Supporting empirical evidence comes from recent studies investigating the neurocognitive effects of multilingual language usage patterns. Specifically, a dual-language context was found to be associated with increased activations in the Anterior Cingulate Cortex (ACC), middle frontal gyrus, and inferior parietal lobule (DeLuca et al. 2020), increased expansions in the left caudate and thalamus (DeLuca et al. 2019), and greater functional connectivity between the ACC and bilateral putamen, and the left caudate and the superior temporal gyrus (Gullifer et al. 2018), regions central to the domain-general control network and language processing (Green and Abutalebi 2013). Additionally, longer exposure to this interactional context appears to be associated with less reliance (i.e., decreased activation and/or expansion) on regions of the control network, possibly reflecting increased efficiency in cognitive control (DeLuca et al. 2019, 2020). Nevertheless, this context of use might not be unique in bringing about neurocognitive adaptations. Although single-language context and dense-code switching engage control mechanisms to a limited extent compared to the dual-language context, they also place high demands on specific control operations. For instance, bilinguals using their languages in single-language contexts appear to rely on frontal and parietal regions to allow for the inhibition of one language over an extended period of time and show increased activation in these regions when compared to monolinguals (Parker Jones et al. 2012). Dense code-switching, on the other hand, is posited to rely heavily on cerebellar structures for the control of morphosyntactic adaptations during opportunistic planning (Green and Abutalebi 2013).

Against this backdrop, LLLL needs to be reconsidered. We might assume that internal factors in language learning interventions (e.g., interactional context, hours of practice) might shape LLLL and its neurocognitive effects as much as experience-based factors do in the case of LM (Keijzer et al. 2023). However, current research has not yet directly compared the effects of LM and LLLL on cognition, brain structure, and brain function. In fact, while modulating factors have been increasingly considered in studies investigating LLLL and LM, the possibility that modulating factors may shape these cognitively stimulating life experiences by triggering distinct effects on neurocognition still needs to be explored. Departing from this perspective, LM and LLLL might be viewed as two instances of language engagement in which internal factors, such as code-switching behavior, proficiency, and duration of training, may (differentially) modulate the degree and scope of the impact that these experiences have on the brain and cognition, possibly leading them to occupy distinct roles in the development of reserve and preservation of cognitive function in older adulthood. Additionally, a novel route for examining the beneficial effects of language engagement is necessary to determine the exact nature of the impact of bilingualism on the preservation of cognitive function. Methodological inconsistencies have led to mixed results



in the past (Antoniou 2025). Thus, a higher level of rigor in discriminating the type of language engagement might shed new light on earlier discrepancies in findings.

## 2 Present study

A rigorous scrutiny of previous literature on the topic is an essential preliminary step in examining the distinct role of LM and LLLL in preventing or delaying cognitive decline due to AD. Specifically, in this systematic review the effects of LM and LLLL on cognition, brain function, and brain structure are compared in older adults at different stages of the AD continuum, from Subjective Cognitive Decline (SCD), Mild Cognitive Impairment (MCI), to AD dementia. By doing so, this project aims to identify whether and to what degree LM and LLLL differ in terms of their impact on CR and BR. To meet this aim, the following research questions form the basis of the systematic review:

1. Do LM and LLLL have different effects on cognition, brain structure, and brain function in older adults with cognitive decline who are diagnosed with or are at risk of AD?
2. Do LLLL and LM engage different cognitive processes and neural networks?
3. Is there a difference in the way LM and LLLL interact with other modulating risk factors that influence CR and BR?
4. Do LM and LLLL differentially impact on cognitive and brain reserve development?

A differential recruitment of neural resources in LM and LLLL can be hypothesized. To some degree, LLLL is analogous to language usage in a single-language context in that the additional language will likely be confined to the training setting, at least for the initial phase of learning. As such, following the ACH premises (Green and Abutalebi 2013), LLLL might be found to involve mainly reactive control processes, leading to a greater recruitment of frontal, parietal, and cortical structures of the control network associated with these processes. These include the ACC and pre-supplementary motor area (governing conflict monitoring), the left prefrontal and inferior cortex (involved in conflict monitoring and interference suppression). Subcortical structures associated with code-switching (i. e., thalamus and basal ganglia) are thus expected to be engaged to a lesser extent in LLLL compared to LM. On the other hand, due to the high variety of experiences that it encompasses, LM is expected to involve both reactive and proactive control processes, thus engaging both cortical and subcortical structures, as well as frontal and parietal regions of the control network.

Differences in the recruitment of neural and cognitive resources might translate to a differential impact of LM and LLLL on CR and BR. We predict that LM will maximize efficiency in general language and executive control processes, leading to the enhancement of associated networks, structures, and functional connections (e. g., circuit composed by the right inferior frontal cortex, thalamus, and basal ganglia involved in salient cue detection (Green and Abutalebi 2013)), while the benefits of LLLL will mostly translate to the enhancement of structures and connections within the frontal and parietal regions of the control network as well as increased efficiency in

reactive control processes. Importantly, an enhancement of frontal brain structures (specifically, prefrontal cortex and IFG) due to LLLL was also predicted by Antoniou and Wright (2017), one of the first studies that hypothesized the protective effect of LLLL against pathological cognitive decline in aging.

Regarding the interaction of LLLL and LM with potentially confounding factors, LM does not require formal education and is also commonly found in economically disadvantaged communities and areas of the world (Gallo and Abutalebi 2024). Moreover, the beneficial effect of LM appears to be greatest in individuals with a lower educational background (Antoniou, Gunasekera, and Wong 2013). On the contrary, access to cognitive interventions or higher awareness of the risks posed by neurodegeneration and the existence of prevention programs might be limited to highly educated and economically advantaged portions of society, thus leading to biases in research. Not coincidentally, it has been observed that participants in cognitive interventions, including LLLL, tend to be highly educated (Poisnel et al. 2018). For this reason, the beneficial effect of LLLL is expected to be mostly observed in individuals with higher socioeconomic status and educational background but could be reported and even more pronounced in participants with lower educational background and socioeconomic status, as in the case of LM, if such participant groups are recruited in intervention studies. Finally, LLLL has been found to have a greater beneficial impact on cognition in older adults with SCD whose cognitive functioning is more compromised compared to older adults who experience SCD but perform within age-typical ranges (Berg 2024), highlighting the effectiveness of LLLL in clinical populations. Therefore, individuals at more severe stages of the AD continuum are expected to benefit more from LLLL.

### 3 Methods

The PubMed, Web of Science, Scopus, and PsycINFO databases were systematically searched on May 26, 2024, and continuously consulted until June 9, 2024. The complete search strings are provided in Appendix 1. In addition to the database search, a manual search of reference lists was conducted on two selected reference articles, Keijzer et al. (2023) and Gallo and Abutalebi (2024), to identify any studies that were not retrieved by the main database search. These recent articles provide a comprehensive account of the literature on LM and LLLL in the context of reserve-enhancement and could therefore reference additional studies.

Preliminary searches revealed a scarcity of studies on LLLL when inclusion criteria were restricted to projects investigating LLLL in the AD continuum. Therefore, to supplement evidence on LLLL, broader inclusion criteria were applied for studies on MCI and SCD populations, allowing studies that did not specify whether the cognitive decline was due to AD to be included in the review.<sup>3</sup> This was applied to both studies on LLLL and LM to guarantee equitable results. Nevertheless, the number of studies retrieved using broader inclusion criteria was still very limited. Thus, an additional search was performed in PubMed on June 3, 2024, retrieving only studies on LLLL in healthy adults aged 65 years and above. Only one database was selected as the additional search was conducted to merely complement the scant evidence on LLLL and explore whether the number of studies would increase in this population. Conse-

3. On the other hand, if the study reported a different etiology, it was excluded from the review.

quently, the main comparison between LLLL and LM was performed while excluding studies on healthy adults.

The title and abstract of each study were screened by one researcher (the first author) to assess eligibility. Eligible studies were selected based on pre-specified inclusion criteria, which were formulated through the PICO framework (Page et al. 2021) and are reported in Table 1. In case of uncertainties, the eligibility was discussed with a second researcher (the second author). After extracting the data, a quality assessment of the included studies was performed to evaluate the risk of bias. During the assessment process, the QualSyst tool for systematic reviews (Kmet, Cook, and Lee 2004) was used, while the results of the risk of bias assessment were evaluated according to criteria elaborated by Lee et al. (2008). The review was conducted in accordance with the PRISMA guidelines (Page et al. 2021). Additionally, the entire review process followed the PRISMA-protocol guidelines (Moher et al. 2015).

Table 1: Inclusion criteria for retrieved studies

|                         |   |
|-------------------------|---|
| Population              | Age: 65 and above<br>Diagnosis: Subjective cognitive decline OR mild cognitive impairment OR dementia due to Alzheimer's disease  |
| Interventions           | Later-life language learning  |
| Comparators             | Bilingual/multilingual population; lifelong, early, and late multilingualism are included   |
| Outcomes                | Cognition (either global cognitive performance or domain-specific cognitive performance) AND/OR brain function AND/OR brain structure   |
| Study design            | Randomized controlled trial AND/OR quasi-experimental studies (e. g., non-randomized controlled studies, before-and-after studies, interrupted time series) AND/OR observational studies (e. g., cohort studies, case-control studies) AND/OR longitudinal studies AND/OR cross-sectional studies |
| Language of the article | English OR Italian  |

## 4 Results

The systematic search yielded 331 citations, of which 330 were retrieved from the database search and 1 from citation searching. Of these, after removing duplicates, 156 were excluded during title/abstract screening and 7 during full-text screening following the inclusion criteria reported in Table 1. As a result, 18 studies were eligible to be included in the review. The additional search yielded 14 citations, of which 3 were included in the review after abstract/title and full-text screening. The search selection process is described fully in Figure 1.



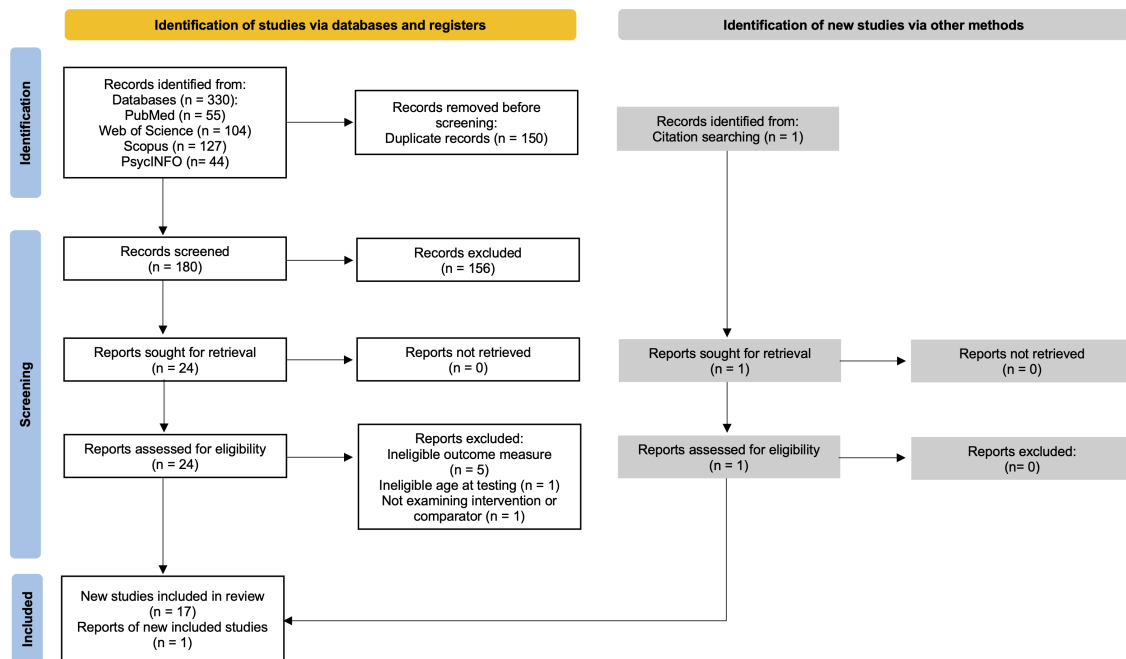


Figure 1: PRISMA 2020 flow diagram of the search and selection process

#### 4.1 Comparing the effects of LLLL and LM on cognition

Appendix 2 summarizes the included studies by specifying the outcome variables, clinical group(s) under investigation, and main results. Most notably, the majority of included studies examined LM, while only 2 investigated LLLL. Additionally, as included studies on LLLL did not investigate brain structure and function, it was impossible to directly compare the effects of LLLL and LM on these outcome measures. Therefore, a direct comparison between LLLL and LM was drawn based on cognition exclusively.

Three studies investigated the impact of bilingualism on cognition in older adults with amnesic MCI (aMCI) (Rosselli et al. 2019), MCI (Kowoll et al. 2015), and MCI due to AD (Voits et al. 2024), and two studies examined the impact of LLLL on cognition in older adults with MCI (Wong et al. 2019; Tigka et al. 2019). The comparison revealed that LM has either a beneficial effect on verbal memory or no effect on memory and executive functioning (EF), while, based on the retrieved papers, we might assume that LLLL seems to have a positive impact on verbal and nonverbal memory and general cognition. In particular, Kowoll et al. (2015) found that the scores of bilinguals on the Trail Making Test (TMT) and Wechsler Memory Scale (WMS), tasks measuring EF and working memory respectively, did not significantly differ from those of monolinguals. Similarly, in the study by Voits et al. (2024), no significant difference was observed between passive bilinguals (speakers whose knowledge of the L2 is confined to comprehension) and active bilinguals (speakers who can use L1 and L2 both in production and comprehension)<sup>4</sup> on episodic memory tasks, namely a visual recognition

4. It is important to note that more researchers are now operationalizing monolingualism and multilingualism on a continuous scale, as in the study by Voits et al. (2024), rather than adopting a dichotomous comparison approach. A more detailed examination of this aspect follows in Section 6.

task and the CERAD Memory Task. By contrast, in the study conducted by Rosselli et al. (2019), active sequential bilinguals significantly outperformed monolinguals on the Loewenstein-Acevedo Scales for Semantic Interference and Learning (LASSI-L), a measure of verbal memory, in subtasks requiring inhibitory control. The bilingual group also performed better on a nonverbal memory task, the Benson Figure test, compared to the monolingual control group, although this difference did not reach significance.

Similar effects emerged from studies on LLLL. Tigka et al. (2019) compared cognitive performance between a language intervention group attending an 18-month English course and a passive control group whose members were not exposed to any cognitive intervention. In Wong et al. (2019), the cognitive performance of a language intervention group learning English for 6 months was contrasted with that of passive and active controls. The active control intervention comprised solving computer-based puzzles and crosswords, while passive controls listened to and read about Chinese music. The former study found a significant improvement in the language intervention group on the Rivermead Behavioural Memory Test (RBMT), measuring memory, and the Rey- Auditory Verbal Learning Test (RAVLT), measuring verbal memory ability, from pre- to post-test compared to the passive control group. The latter study revealed improved performance in attention, working memory, and general cognition from pre- to post-test and lexical retrieval from post-test to follow-up, but independent of intervention group. Specifically, the language intervention showed greater — albeit not significant — improvement in general cognition, measured through the Alzheimer Disease Assessment Scale — Cognitive subscale (ADAS-Cog), than the active and passive control groups.

Concerning confounding factors, all the studies controlled for educational attainment when performing statistical analyses. By comparing the education level between studies on LM and LLLL, it emerges that — in two of the three LM studies — the bilingual groups had more years of education (mean = 14.76 in Rosselli et al. (2019); mean = 12.5 in Kowoll et al. (2015)) compared to the intervention group recruited by Tigka et al. (2019) (mean = 11.83). Lower educational attainment was reported for the bilingual group in only one LM study, namely the one by Voits et al. (2024) (mean = 7.87 years). Data on educational attainment were not reported in the second study on LLLL by Wong et al. (2019).

## 4.2 Risk of bias assessment

The quality assessment performed through the QualSyst tool (Kmet, Cook, and Lee 2004) revealed a considerably low risk of bias. All the included studies were classified as strong in terms of quality (score > 0.8). Although this did not strongly influence the final quality score, it is also important to note that many included studies were underpowered mostly due to difficulties in participant recruitment.

## 4.3 The effect of LLLL on cognition in healthy older adults

To supplement the evidence on LLLL, the search was expanded to studies in which a language intervention was offered to healthy older adults. This follows from the fact that many LLLL interventions may well aim to safeguard cognitive health in older adulthood rather than present a treatment after decline onset (Klimova 2018). Nevertheless, only 3 studies were identified involving healthy older adults ( $\geq 65$  years of

age, in line with the other studies found), all of which examined only the effect of LLLL on cognition, without reporting brain structural and functional measures (Berggren et al. 2020; Meltzer et al. 2021; Valis et al. 2019). Moreover, in all studies, LLLL was not associated with any changes in cognitive performance from pre-intervention to post-intervention, and no significant differences in cognitive performance were reported between the intervention and control groups. These findings should be treated with caution; these studies were retrieved through an additional, limited search to complement evidence on LLLL in AD, and a more detailed search on several databases might yield more results. However, the need for further research in this area is compelling, especially given the lack of consistent results. The studies are summarized in Appendix 3.

## 5 Discussion

The scarcity of studies investigating LLLL in older adults experiencing cognitive decline due to AD hindered a holistic and comprehensive comparison of the effects of LLLL and LM and cognition, brain function, and brain structure within the AD continuum. Nevertheless, it was possible to directly compare data on the impact of LLLL and LM on cognitive performance in older adults with MCI. The following paragraphs provide a detailed account of the current findings by revisiting the research questions that form the basis of this review.

### 5.1 Do LLLL and LM have a different impact on cognition and reserve?

Similar trends were observed relating to LLLL and LM's impact on cognition. On the one hand, three of the five included studies did not find any advantages in EF, working memory, or episodic memory in cognitively impaired older adults as a consequence of being bilingual (Kowoll et al. 2015; Voits et al. 2024) or learning a foreign language (Wong et al. 2019). On the other hand, two studies reported a positive effect of LLLL (Tigka et al. 2019) and LM (Rosselli et al. 2019) on the ability to perform nonverbal memory tasks, as well as memory tasks requiring executive control mechanisms, such as interference suppression and inhibitory control.

Variability in bilingual experiences appears to account for the different findings attested in the LM realm. Following the ACH (Green and Abutalebi 2013) and the Dynamic Restructuring Model (Pliatsikas 2020), an environment where the majority of the population has some degree of knowledge of both languages, allowing opportunistic planning, like in Voits et al. (2024), and the prolonged use of multiple languages throughout life, which characterized bilinguals in Kowoll et al. (2015), might limit the demands on cognitive control processes. Contrarily, bilingual participants in Rosselli et al. (2019) were sequential, mostly late bilingual speakers of Spanish and English, who acquired English at around 12 years of age. Although the context of language use was not specified, later acquisition and use of the L2 might signal that this population was unbalanced in their bilingual use patterns, with Spanish being considered their dominant language by 62 % of the participants. At this stage of bilingual experience, demands on brain regions involved in executive control are particularly taxing, making neurocognitive adaptations in the control network to achieve greater efficiency highly likely (Pliatsikas 2020). In the study by Rosselli and colleagues, the superior performance of bilinguals on tasks tapping into inhibitory control mechanisms might

thus indicate an enhancement of the executive control network resulting from this type of bilingual experience. Not coincidentally, in this bilingual group, scores on memory tests were positively correlated with scores on the Stroop Color-Word test, which measures the ability to suppress interference (Scarpina and Tagini 2017).

We predicted that higher demands on EF and—particularly—control processes might also be expected in LLLL. Indeed, at the initial stages of language learning, given lower levels of L2 proficiency, L2 production might be highly dependent on the inhibition of the non-target language (Baum and Titone 2014), as was hypothesized. This hypothesis was supported by the findings in Tigka et al. (2019), revealing higher scores for the language intervention group compared to passive controls that were not involved in any cognitive intervention on memory tasks assessing the ability to learn new information (Wilson 2008) and the effect of interference on recall (Bean 2011). However, this was not the case in Wong et al. (2019), who did not report any differences in cognitive performance between intervention groups. It might be plausible that, in the latter study, differences in performance on tasks measuring working memory, attention, and lexical retrieval were not observed because, contrary to the passive control in Tigka et al. (2019), the active and passive control groups also took part in other cognitively stimulating activities, namely solving computer-based puzzles and listening to Chinese music, which might have had a positive impact on cognition, masking any effect of LLLL. In fact, performance on neuropsychological tests improved from pre- to post-intervention and follow-up independent of intervention group.

Taking these considerations into account in the comparison of LLLL and LM's impact on cognition, it appears that LLLL and—under specific conditions—LM increase the demands on cognitive control processes which, in turn, become more efficient as indexed by enhanced cognitive performance. However, to determine whether the scope of this adaptation varies between LM and LLLL, the tasks on which an advantage was observed must be directly compared. In Rosselli et al. (2019), bilinguals outperformed monolinguals on one subtask of the LASSI-L, which measures the ability to recover from proactive semantic interference and as such taps into higher-order monitoring skills (Rosselli et al. 2019). The intervention group in Tigka et al. (2019) showed a superior performance compared to controls on the RAVLT, a memory test that through its subtasks also assesses the effect of both proactive and retroactive interference in some of its subtasks (Malloy-Diniz et al. 2007). Based on these findings, the prediction that LLLL would mainly involve and enhance reactive control processes, while LM would engage both reactive and proactive control is thus refuted.

Nonetheless, this result should be interpreted with caution. Most importantly, the small number of included studies greatly limits the generalizability of the findings. Additionally, as the study by Tigka et al. (2019) mainly focused on memory capacity, the specific RAVLT subtasks on which the intervention group outperformed controls were not reported. Therefore, it was not possible to determine whether the enhancement of control was observed in both proactive and reactive mechanisms. This was also the case in studies on LLLL and LM that did not reveal any differences between experimental and control groups, thus impeding further clarification. It was also difficult to observe any differences or similarities in the way LLLL and LM impact reserve. The studies included in the main comparison almost exclusively investigated the effects of

LLLL and LM on cognition,<sup>5</sup> without reporting on any structural and functional brain measures. Thus, it was impossible to examine whether the observed cognitive benefits could be attributed to CR or BR. Furthermore, while LM, being a lifelong experience, serves as a continuous form of neurocognitive training and drives long-lasting neural potentiation, the beneficial effect of LLLL on cognition might be limited in time due to the relatively brief duration and low intensity of the interventions (Meltzer et al. 2021). Both in Wong et al. (2019) and in Tigka et al. (2019), a post-intervention assessment of the impact of LLLL on cognition was conducted. Nonetheless, only Wong et al. (2019) specified the timing of the follow-up, which occurred three months after training ended, and, based on the data reported in both studies, it remains unclear whether LLLL provided a protracted beneficial effect over the years. The only general conclusion that can be reached on the basis of the studies that were analyzed is that increasing demands on executive control processes seem a common denominator of reserve enhancement in LLLL and LM, thus providing further support for the theoretical accounts of the mechanisms involved in reserve development.

## **5.2 Neurocognitive adaptations through language engagement**

### **5.2.1 Cognition**

No direct comparison of the effects of LM and LLLL on cognition in other clinical groups besides MCI could be made. However, the LM studies that did include AD dementia and SCD as clinical groups yielded meaningful results, highlighting the importance of experience-related factors when evaluating the role of bilingualism in reserve development. Clare et al. (2016), for instance, analyzed the effect of early and simultaneous bilingualism on multiple aspects of EF in the early stages of AD dementia. They found no significant differences between English-Welsh bilinguals and English monolinguals in mental flexibility, working memory, inhibition, and management of response conflict. Similar to other studies where no bilingual advantage was found (Kowoll et al. 2015; Voits et al. 2024), the researchers attributed this lack of language-group differences to the sociolinguistic context from where the sample was recruited, Wales. In this region, Welsh monolinguals, who were not included in the study, tend to use English in everyday interaction. Thus English-Welsh bilinguals might show less reliance on inhibitory control, as English intrusions are 'acceptable'. However, the bilinguals were more cognitively impaired at the time of dementia diagnosis than their monolingual peers. This element might be an indicator of higher reserve in this language group, who continued to perform at similar levels of monolinguals on EF tasks despite being significantly more impaired in general cognition, in line with the cognitive reserve model proposed by Stern (2009, 2012). Alternatively, cultural differences in the perception of dementia and reliance on family members for care has been reported to delay consulting a specialist in Moroccan, Surinamese, and Turkish immigrants (Vissenberg et al. 2018); further investigation of these cultural aspects in the Welsh context might thus be needed.

While the study by Clare et al. (2016) added to the importance of the context of bilingual language use, a recent study by Ballarini et al. (2023) explored the role of

5. Voits et al. (2024) investigated brain structure in addition to cognitive performance. However, as none of the other studies reported brain structure measures to compare, the brain structure findings are not included in this review.



bilingual experience on cognition at various lifespan stages. More specifically, different bilingual groups were identified depending on the life stage at which multiple languages were actively used. Using the same criterion, a monolingual counterpart was identified for each bilingual group member, matched for age, thus maintaining a dichotomous operationalization of bilingualism. The findings showed that early bilingualism was associated with enhanced performance in learning and memory, language, EF, and working memory, and bilingualism in middle life with learning and memory only. No significant effects on cognition were found for lifelong bilingualism or bilingualism at the mid-life stage but a cumulative effect of bilingual experience (i.e., the degree of bilingualism throughout life) was observed on all cognitive domains, including visuospatial abilities. Besides showing that the life stage at which multiple languages are actively used might be relevant when investigating the effects of LM on cognition, of the 18 studies included in this review, this is the only study that investigated the role of bilingualism in SCD. It is crucial to specify that no distinction was made between clinical groups, meaning that SCD participants were grouped with healthy adults in statistical analyses. Nevertheless, this study might encourage further work on (pre)clinical populations.

### 5.2.2 Brain function

The findings gathered from LM studies analyzing brain function aligned with our predictions. Despite variability in the adopted definitions of bilingualism and the type of bilingual experiences characterizing the recruited samples, the studies by Kowoll et al. (2016), Sala et al. (2022), and Perani et al. (2017) revealed that, at equivalent levels of cognitive performance, bilinguals with AD dementia and MCI showed more severe cerebral hypometabolism in frontal, parietal, and temporal brain regions, as well as subcortical structures. Specifically, severe hypometabolism in the IFG, ACC, putamen, and cerebellum was consistently reported across studies.

Cerebral glucose hypometabolism is indicative of reduced neural activity (Madsen, Hvidsten, and Andersen 2023) and has been commonly found in parieto-temporal and frontal cortices in AD (Blázquez et al. 2022). A significant decrease in neural activity in the presence of AD pathology when compared to age-matched or younger monolinguals thus suggests that the bilingual groups experienced more severe AD neuropathology at the time of testing. However, the comparable levels of cognitive performance between language groups indicate that LM likely led to a higher degree of CR in bilingual participants, allowing them to perform on a par with their monolingual peers on cognitive measures.

Moreover, reduced neural activity was found in neural systems central to the executive control network and related to both proactive and reactive control processes. The ACC is known to be highly activated in language switching (Green and Abutalebi 2013), when there is a major demand on the ability to detect response conflict, and to signal the need for top-down control to other systems within the control network, such as the prefrontal cortex (Abutalebi and Green 2007). In particular, in the prefrontal cortex, the IFG, has been reported to regulate response inhibition, specifically through the fronto-striatal pathway, which connects the prefrontal cortex to subcortical structures in the basal ganglia, including the putamen (Zhuang et al. 2023), and the cerebellum (Heyder, Suchan, and Daum 2004). These structures, in turn, might be engaged to different extents depending on the context/pattern of language

use. For instance, the putamen plays a pivotal role in motor control and is involved in set-shifting, task engagement/disengagement, and language selection (Abutalebi and Green 2007), operations crucial for switching in dual-language contexts, while the cerebellum appears to be highly activated in dense code-switching through morphosyntactic control (Green and Abutalebi 2013). The differing bilingual experiences reported in the reviewed studies might thus have extensively engaged multiple brain structures and functional connections within the control network associated with both reactive and proactive control processes. By doing so, the efficiency of these brain structures and functional connections was enhanced (i. e., higher CR). In turn, a greater degree of efficiency in these structures and functional connections might have led bilinguals to perform similarly to monolinguals on cognitive testing, despite the former being more severely impaired in these very same structures, thus offering neuroprotection in aging.

This idea was further corroborated by the positive association between the degree of bilingualism (i. e., prolonged and more active use of L2) and hypometabolism in AD dementia found in Sala et al. (2022), as well as the increase in connectivity within the language and executive control network consistently reported in Marin-Marín et al. (2021), Perani et al. (2017), and Sala et al. (2022) for the bilingual groups. Specifically, increased functional connectivity was found between anterior and posterior regions of the language and executive control network, including the ACC, IFG, and basal ganglia, in bilinguals with MCI and AD dementia. These findings are consistent with the predictions of the CR model (Stern 2009, 2012), suggesting that different experiences within LM contribute — especially when the L2 is used more frequently — to the development of CR by posing additional demands on the control network.

### 5.2.3 Brain structure

Similarly to functional brain changes, the included LM studies appear to confirm our hypotheses regarding LM's impact on brain structure. More specifically, LM was found to generate structural changes in the IFG (Calvo et al. 2023; Duncan et al. 2018; Torres et al. 2022), the ACC (Calvo et al. 2023), and the cerebellum and thalamus (Duncan et al. 2018; Raji et al. 2020), which, together with the prefrontal cortex and basal ganglia, allow operations such as salient cue detection, response inhibition, task engagement/disengagement and are particularly active in dual-language contexts (Green and Abutalebi 2013).

A second trend emerging from the studies included in our review was the association between LM and greater atrophy in structures commonly affected by AD and majorly related to memory. These include the superior parietal lobule, involved in episodic memory and affected during the conversion from MCI to AD dementia (Calvo et al. 2023), the lingual and supramarginal gyrus (Costumero et al. 2020), affected by AD and related to visual and short-term memory, respectively (Guidali et al. 2019; Zhang et al. 2016). Greater atrophy was also found in the medial-temporal lobes (Schweizer et al. 2012), specifically the hippocampus (Duncan et al. 2018), and white matter tracts part of the hippocampal-diencephalic-cingulate networks (Marin-Marín et al. 2020), regions particularly affected by AD even at early stages (Squire, Stark, and Clark 2004) and central to declarative memory (Squire, Stark, and Clark 2004).

Importantly, the patterns observed in disease-related areas and structures central to the control network presented above appear to be related to the role of LM

in reserve enhancement; bilinguals with MCI due to AD in Schweizer et al. (2012) showed greater atrophy and a significant decrease in GM density in areas affected by AD or relevant for executive control mechanisms, while performing on a par with monolingual controls on cognitive tasks. Therefore, in these groups, LM has likely contributed to the development of CR by maximizing the efficiency of control networks, thus counterbalancing disease-related atrophy affecting either memory areas or the very same structures involved in executive control, in agreement with Stern's CR model. CR also seems to account for the findings on older adults with SCD and at high risk of AD in Ballarini et al. (2023). In that study, no GM volume reductions were found in bilingual participants when compared to monolingual peers. However, bilingualism in the early and middle life stages was associated with increased scores on neuropsychological measures of memory, language, EF, and visuospatial abilities, thus suggesting that LM contribution to CR might be evident in better cognitive performance when bilinguals and monolinguals are matched on brain structural levels, again in line with Stern's CR model.

However, some included studies also reported the opposite pattern, namely larger GM volume in the bilingual rather than the monolingual group at equal levels of cognitive impairment. This was the case in Raji et al. (2020), who reported larger brain volumes in the thalamus, frontal and temporal lobes for bilinguals in a cohort affected by AD dementia, and in Torres et al. (2022), reporting greater GM volume in regions related to language processing and EF in bilinguals with MCI and AD dementia. Specifically, increased volume was found in the IFG in both disease groups and orbitofrontal cortices in the dementia group, regions fundamental for inhibitory control (Bryden and Roesch 2015), with bilingualism being associated with reduced interference on the Stroop Color-Word Interference test (Torres et al. 2022).

The immigration status of participants might account for these seemingly contradictory results. In the studies investigating brain structure reported above, the bilingual groups were comprised mostly or entirely of immigrants, and immigration status was not analyzed as a possible confound. Contrarily, immigration status was controlled for in Calvo et al. (2023), who reported decreases in GM density in their bilingual sample. This factor might have thus influenced the effect of LM on brain structure that was observed in Raji et al. (2020) and Torres et al. (2022). However, no information concerning the participants' migratory background was reported in Schweizer et al. (2012) and Ballarini et al. (2023), thus limiting this interpretation. Alternatively, variability in the analyzed structural measures and neuroimaging techniques might better explain the contradictory findings in studies on brain structure.

What is more, these findings may not be as contradictory as they appear. The volume increases found by Raji et al. (2020) and Torres et al. (2022) can be interpreted as a difference in the level of BR as a function of LM. In particular, by increasing demands on neural networks related to multilingual language processing and, specifically, control, LM appears to boost BR capacity, generating the observed advantage on cognitive tasks measuring cognitive control. On the other hand, the findings by Schweizer et al. (2012), Calvo et al. (2023), and Ballarini et al. (2023) were interpreted above as indicative of higher CR in the bilingual group. Thus, all the analyzed studies likely point to a beneficial effect of LM on reserve development which becomes crucial to sustain cognitive functioning in pathological aging, with merely the type of reserve mechanism rendering differences.

Interestingly, CR and BR were also reported to operate synergistically across time in bilinguals diagnosed with aMCI and AD dementia. In a cross-sectional study, Duncan et al. (2018) found that, within a sample of bilinguals and monolinguals matched on episodic memory performance, bilinguals with aMCI showed greater GM density and cortical thickness than monolinguals, while the reverse was found in the dementia group. These results indicate that LM might have contributed to both CR and BR, and that CR could come into play once BR capacity has been fully depleted. However, a longitudinal study by Costumero et al. (2020) reported no language-group differences in cognitive performance and more severe volume loss in bilinguals at baseline, followed by faster cognitive decline and atrophy in the monolingual group at a 7-month follow-up, suggesting that an inverted temporal sequence in the utilization of BR and CR is also possible. Again, a difference in the analyzed brain structural measures might explain these contradictory results, with the former study investigating GM density and the latter GM volume.

### 5.3 The role of confounding factors

Concerning the role of confounding factors in LLLL and LM, our hypothesis was confirmed; following standard criteria for the classification of educational attainment (UNESCO Institute for Statistics 2012), in most of the reviewed LLLL studies, including studies on healthy older adults, participants had a high level of education, from 16 up to 17 years on average. However, Tigka et al. (2019) reported a positive effect of LLLL on memory and EF in older adults diagnosed with MCI and with a lower educational background (12 years on average). This suggests that LLLL can be beneficially implemented in the general population, independent of their educational background, if people with both high and low levels of education are recruited. Moreover, LLLL was found to be more effective at stimulating cognitive functioning in older adults with greater cognitive decline (Berg 2024), and, this review showed that it is indeed in people with a lower educational background that LLLL generates cognitive benefits, similar to what has been previously observed for LM (Antoniou, Gunasekera, and Wong 2013) and that might thus be generalizable to language engagement. Concerning LM, however, studies included older adults with between 7 to 15 years of education on average, mostly finding a beneficial effect on neurocognition regardless of educational background.

Together with education and occupational status, which are commonly used as proxy measures of reserve (Song, Stern, and Gu 2022), additional factors were consistently reported in the reviewed studies. These include immigration status for LM, and motivation and social interaction for LLLL. Immigration is frequently associated with bilingualism (Duncan et al. 2018) and, therefore, it is likely to be analyzed in studies investigating LM. Similarly, socializing is typically considered an additional benefit of bilingualism that could contribute to reserve enhancement (Evans et al. 2018), while motivation is considered a key factor for participant adherence (Keijzer et al. 2023) and the success of the language training course (Ploeg, Keijzer, and Lowie 2023). However, contrarily to immigration for LM, both motivation and social interaction were not examined as potential mediators of LLLL's impact on cognition, a hypothesis that future studies on LLLL should further investigate. Additionally, future research on LM might also investigate whether multilingual speakers acquired their languages



through formal education, an additional confounding factor that might modulate LM experience and its effect on neurocognition (Bruin 2019).

## 6 Conclusion and future directions

The neurocognitive adaptations associated with language engagement are acquiring particular attention in research on dementia prevention due to their potential in the maintenance of healthy levels of cognitive functioning in (pathological) aging. However, the role of bilingualism as a reserve-enhancing factor remains debated. This systematic review has addressed the controversy surrounding bilingualism by examining the distinct roles of LLLL and LM in reserve development in older adults who suffer from cognitive decline, suggesting that contrasting results might originate from an unaccounted variability in bilingual experience. The review revealed that LM contributes to the development of both BR and CR by engaging and, consequently, enhancing domain-general cognitive control in its entirety, including reactive and proactive control mechanisms. This advantage seems to benefit multilingual older adults alongside every stage of the AD continuum, allowing them to sustain greater neuropathology and preserve or even increase their cognitive abilities. One study on LLLL also showed a beneficial effect of linguistic intervention on tasks that tap into reactive and proactive control processes, but evidence is extremely meager, especially within clinical populations, and limited to analyses of memory abilities rather than EF and their neural substrates, although this cognitive domain is where the theorized benefits of LLLL should be observed. This work has some limitations. Studies were assessed for inclusion criteria only by the first author, although in consultation with the second author, and one study (Tigka et al. 2019) was retrieved through citation searching. Additionally, new papers on LM and LLLL might have been published since June 2024 as, for instance, a study comparing the effect of LLLL on cognition with other cognitively stimulating activities in healthy older adults (Brouwer et al. 2025). Nevertheless, handsearching has been acknowledged as a valid methodology in healthcare research (Hopewell et al. 2007) and standard criteria for conducting systematic reviews were carefully adopted during the entire review process, suggesting the overall soundness of the current findings.

This review has also highlighted meaningful discussion points in this research area that warrant further investigation. The most evident finding is the scarcity of studies analyzing the impact of language engagement on neurocognition in older adults in the AD continuum. Although dementia prevention represents one of the major societal challenges of our times and AD is recognized as the main cause of dementia, there is a general lack of studies on this population in research on LM, especially at the early stages of the disease progression like SCD. This research gap is even more evident in the realm of LLLL interventions. This scarcity of studies has hampered the analyses conducted in this review and urges caution when interpreting the current findings but, most importantly, highlights the need for further research on the role of both LM and LLLL in reserve development and the neuroprotection they might offer against AD-related cognitive decline. More generally, filling this gap in the literature is also necessary to resolve inconsistencies in language engagement research. Difficulties in recruiting and testing participants who are experiencing pathological neurocognitive changes, especially for the implementation of cognitive interventions, might have driven the current lack of studies; however, the fact that, nonetheless,



studies on LLLL and LM have already been successfully conducted in this population, is promising.

Another aspect of current research that emerged in this review was the variability in study design and terminology. First, it was noted that different diagnostic and classification tools were used to recruit group participants depending on their clinical status and linguistic background. Bilingualism, for instance, was often defined as the regular and active use of more than one language, but different questionnaires and scales were used to assess linguistic background. Moreover, no clear definition of monolingualism was reported in the majority of the studies nor was there a clear description of the context of language use, although its role in neurocognitive adaptations is now commonly accepted. Similarly, MCI and AD dementia were diagnosed based on slightly different clinical criteria. Neuropsychological tests for the assessment of cognition also differed often among studies, even for the testing of domain-specific cognitive abilities such as EF. These heterogeneities in diagnostic and testing tools, together with the lack of granularity in the description of LM and the participants' background (e.g. migratory background), might weaken our understanding of the type of multilingual experience and the cognitive control processes that specific experiences might have engaged, as well as undermine the reproducibility of findings.

Secondly, it was observed that the definitions of BR and CR did occasionally overlap. Raji et al. (2020) found evidence of BR in their bilingual sample but interpreted the structural changes induced by bilingualism as CR or neural reserve. On the other hand, Torres et al. (2022), who also found evidence of BR, interpreted their findings as BR but used the term neural reserve to refer to it. It is important to notice that, albeit being the most influential, Stern's definition of reserve is not unique (Ansado et al. 2013). Nevertheless, consistency in the operationalization of reserve might be beneficial for the comparability of findings. Furthermore, the reviewed studies on LLLL differed in terms of control groups (active vs passive controls), intervention modalities, and assessment frequency (post-test or follow-up), and some of the studies on LM (Costumero et al. 2020; Marin-Marín et al. 2020; Marin-Marín et al. 2021; Voits et al. 2024) opted for the operationalization of bilingualism as a continuum, differences that might also impact the generalization of findings. In particular, the dichotomous comparison of bilingualism versus monolingualism is being progressively abandoned in favour of a conceptualization of LM as a spectrum. This shift enables a more fine-grained analysis when examining the impact of language engagement on reserve, capturing the complexity that this experience entails (Voits, DeLuca, and Abutaleb 2022). Yet, persistent variability in terminology among the subset of reviewed studies that treated LM as a continuous variable underlines the need for establishing a standardized approach to the study of LM, especially in terms of its definition and assessment. Following a definite study design is crucial to understanding the role of LM in reserve enhancement and thus should warrant immediate consensus within the field.

Future work would do well to avoid the high degree of terminological and design heterogeneity revealed by this review, as well as offer greater granularity in reporting participants' background, by developing standard research criteria for the investigation of the neurocognitive benefits of language engagement in clinical populations. This would allow greater control over possible confounding factors and help explain the variability in research findings that is oftentimes reported in studies on LM and LLLL. In future research, the effects of LLLL and LM on the cognitive level, functional

brain level, and structural brain level could be examined and directly compared in multisite studies involving older adults in the AD continuum. By adopting structured procedures and investigating this research topic across multiple environments, evidence on the role of bilingualism in preserving cognitive functioning later in life would be consolidated, ending the current debate and paving the way for applications of LM and LLLL directed at preventing and subsiding the risk of dementia, thus fostering healthy aging.

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## **Ethics statement**

Since the analysis relied exclusively on previously published data, ethics approval was not required for this systematic review. All studies included in this review obtained the official approval of an ethics committee, included an ethical statement, and/or were conducted after receiving informed consent from all participants. Only the studies by Ballarini et al. (2023), Raji et al. (2020), Rosselli et al. (2019), and Voits et al. (2024) did not report any information about these criteria.

## **Conflict of interest**

The authors have no conflict of interest to declare.

## Appendix 1: Final search strings

### PubMed (55 retrieved citations)

((("lifelong multilingual\*" [Title/Abstract]) OR ("lifelong bilingual\*" [Title/Abstract]) OR ("lifelong multilingual experience\*" [Title/Abstract]) OR ("multilingual experience\*" [Title/Abstract]) OR ("bilingualism" [Title/Abstract]) OR ("multilingualism" [Title/Abstract]) OR ("later-life language learning" [Title/Abstract]) OR ("late-life language learning" [Title/Abstract]) OR ("language intervention\*" [Title/Abstract]) OR ("foreign language learning" [Title/Abstract]) OR ("foreign language training" [Title/Abstract]) OR ("third-age language learning" [Title/Abstract]) OR ("L2 training" [Title/Abstract]) OR ("foreign language acquisition" [Title/Abstract]) OR ("foreign-language acquisition" [Title/Abstract]) OR ("second language acquisition" [Title/Abstract]) OR ("second-language acquisition" [Title/Abstract])) AND (("brain structural change\*" [Title/Abstract]) OR ("structural brain change\*" [Title/Abstract]) OR ("structural change\*" [Title/Abstract]) OR ("brain structure" [Title/Abstract]) OR ("cortical thickness" [Title/Abstract]) OR ("grey matter volume" [Title/Abstract]) OR ("grey matter density" [Title/Abstract]) OR ("gray matter volume" [Title/Abstract]) OR ("gray matter density" [Title/Abstract]) OR ("hippocampal volume\*" [Title/Abstract]) OR ("brain atrophy" [Title/Abstract]) OR ("brain activit\*" [Title/Abstract]) OR ("neural activit\*" [Title/Abstract]) OR ("cognitive function\*" [Title/Abstract]) OR ("functional connectivity" [Title/Abstract]) OR ("white matter integrity" [Title/Abstract]) OR ("white matter structure" [Title/Abstract]) OR ("white matter tract\*" [Title/Abstract]) OR ("fractional anisotropy" [Title/Abstract]) OR ("radial diffusivity" [Title/Abstract]) OR ("axial diffusivity" [Title/Abstract]) OR ("neural connectivity" [Title/Abstract]) OR ("brain metabolism" [Title/Abstract]) OR ("metabolic connectivity" [Title/Abstract]) OR ("cerebral glucose metabolism" [Title/Abstract]) OR ("cognitive performance\*" [Title/Abstract]) OR ("cognition" [Title/Abstract]) OR ("neuropsychological data" [Title/Abstract]) OR ("cognitive functioning" [Title/Abstract]) OR ("mental health" [Title/Abstract]) OR ("executive function\*" [Title/Abstract]) OR ("cognitive abilit\*" [Title/Abstract]) OR ("mini-mental state examination" [Title/Abstract]) OR ("MMSE" [Title/Abstract]) OR ("cognitive reserve" [Title/Abstract]) OR ("brain reserve" [Title/Abstract])) AND (("Alzheimer's disease" [Title/Abstract]) OR ("AD" [Title/Abstract]) OR ("Alzheimer" [Title/Abstract]) OR ("probable AD" [Title/Abstract]) OR ("Alzheimer's dementia" [Title/Abstract]) OR ("Alzheimer dementia" [Title/Abstract]) OR ("dementia" [Title/Abstract]) OR ("AD dementia" [Title/Abstract]) OR ("AD-dementia" [Title/Abstract]) OR ("dementia due to AD" [Title/Abstract]) OR ("mild cognitive impairment" [Title/Abstract]) OR ("MCI" [Title/Abstract]) OR ("aMCI" [Title/Abstract]) OR ("a-MCI" [Title/Abstract]) OR ("MCI due to AD" [Title/Abstract]) OR ("subjective cognitive decline" [Title/Abstract]) OR ("SCD" [Title/Abstract]) OR ("subjective memory impairment" [Title/Abstract]) OR ("cognitive complaint\*" [Title/Abstract]) OR ("cognitive concern\*" [Title/Abstract]) OR ("memory complaint\*" [Title/Abstract]) OR ("memory concern\*" [Title/Abstract]))

Refined by: ARTICLE LANGUAGE (English or Italian) and AGE ('Aged: 65+ years' or '80 and over: 80+ years')

### Web of Science (104 retrieved citations)

TS=((("lifelong multilingual\*" OR "lifelong bilingual\*" OR "lifelong multilingual experience\*" OR "multilingual experience\*" OR "bilingualism" OR "multilingualism" OR

"later-life language learning" OR "late-life language learning" OR "language intervention\*" OR "foreign language learning" OR "foreign language training" OR "third-age language learning" OR "L2 training" OR "foreign language acquisition" OR "foreign-language acquisition" OR "second language acquisition" OR "second-language acquisition")) AND TS= (("brain structural change\*" OR "structural brain change\*" OR "structural change\*" OR "brain structure" OR "cortical thickness" OR "grey matter volume" OR "grey matter density" OR "gray matter volume" OR "gray matter density" OR "hippocampal volume\*" OR "brain atrophy" OR "brain activit\*" OR "neural activit\*" OR "cognitive function\*" OR "functional connectivity" OR "white matter integrity" OR "white matter structure" OR "white matter tract\*" OR "fractional anisotropy" OR "radial diffusivity" OR "axial diffusivity" OR "neural connectivity" OR "brain metabolism" OR "metabolic connectivity" OR "cerebral glucose metabolism" OR "cognitive performance\*" OR "cognition" OR "neuropsychological data" OR "cognitive functioning" OR "mental health" OR "executive function\*" OR "cognitive abilit\*" OR "mini-mental state examination" OR "MMSE" OR "cognitive reserve" OR "brain reserve")) AND TS= (("Alzheimer's disease" OR "AD" OR "Alzheimer" OR "probable AD" OR "Alzheimer's dementia" OR "Alzheimer dementia" OR "AD dementia" OR "AD-dementia" OR "dementia due to AD" OR "mild cognitive impairment" OR "MCI" OR "aMCI" OR "a-MCI" OR "MCI due to AD" OR "subjective cognitive decline" OR "SCD" OR "subjective memory impairment" OR "cognitive complaint\*" OR "cognitive concern\*" OR "memory complaint\*" OR "memory concern\*"))

Refined by: DOCUMENT TYPE (Article or Editorial Material or Early Access or Book Chapters) and LANGUAGES (English)

### **Scopus (127 retrieved citations)**

TITLE-ABS-KEY ( ( "lifelong multilingual\*" OR "lifelong bilingual\*" OR "lifelong multilingual experience\*" OR "multilingual experience\*" OR "bilingualism" OR "multilingualism" OR "later-life language learning" OR "late-life language learning" OR "language intervention\*" OR "foreign language learning" OR "foreign language training" OR "third-age language learning" OR "L2 training" OR "foreign language acquisition" OR "foreign-language acquisition" OR "second language acquisition" OR "second-language acquisition" ) AND ( "brain structural change\*" OR "structural brain change\*" OR "structural change\*" OR "brain structure" OR "cortical thickness" OR "grey matter volume" OR "grey matter density" OR "gray matter volume" OR "gray matter density" OR "hippocampal volume\*" OR "brain atrophy" OR "brain activit\*" OR "neural activit\*" OR "cognitive function\*" OR "functional connectivity" OR "white matter integrity" OR "white matter structure" OR "white matter tract\*" OR "fractional anisotropy" OR "radial diffusivity" OR "axial diffusivity" OR "neural connectivity" OR "brain metabolism" OR "metabolic connectivity" OR "cerebral glucose metabolism" OR "cognitive performance\*" OR "cognition" OR "neuropsychological data" OR "cognitive functioning" OR "mental health" OR "executive function\*" OR "cognitive abilit\*" OR "mini-mental state examination" OR "MMSE" OR "cognitive reserve" OR "brain reserve" ) AND ("Alzheimer's disease" OR "AD" OR "Alzheimer" OR "probable AD" OR "Alzheimer's dementia" OR "Alzheimer dementia" OR "AD dementia" OR "AD-dementia" OR "dementia due to AD" OR "mild cognitive impairment" OR "MCI" OR "aMCI" OR "a-MCI" OR "MCI due to AD" OR "subjective cognitive decline" OR "SCD"

OR "subjective memory impairment" OR "cognitive complaint\*" OR "cognitive concern\*" OR "memory complaint\*" OR "memory concern\*") )

Refined by: LANGUAGE (English)

### **PsycINFO (44 retrieved citations)**

((TI("lifelong multilingual\*" OR "lifelong bilingual\*" OR "lifelong multilingual experience\*" OR "multilingual experience\*" OR "bilingualism" OR "multilingualism" OR "later-life language learning" OR "late-life language learning" OR "language intervention\*" OR "foreign language learning" OR "foreign language training" OR "third-age language learning" OR "L2 training" OR "foreign language acquisition" OR "foreign-language acquisition" OR "second language acquisition" OR "second-language acquisition")) OR (AB("lifelong multilingual\*" OR "lifelong bilingual\*" OR "lifelong multilingual experience\*" OR "multilingual experience\*" OR "bilingualism" OR "multilingualism" OR "later-life language learning" OR "late-life language learning" OR "language intervention\*" OR "foreign language learning" OR "foreign language training" OR "third-age language learning" OR "L2 training" OR "foreign language acquisition" OR "foreign-language acquisition" OR "second language acquisition" OR "second-language acquisition")) OR (SU("lifelong multilingual\*" OR "lifelong bilingual\*" OR "lifelong multilingual experience\*" OR "multilingual experience\*" OR "bilingualism" OR "multilingualism" OR "later-life language learning" OR "late-life language learning" OR "language intervention\*" OR "foreign language learning" OR "foreign language training" OR "third-age language learning" OR "L2 training" OR "foreign language acquisition" OR "foreign-language acquisition" OR "second language acquisition" OR "second-language acquisition")))) AND ((TI("brain structural change\*" OR "structural brain change\*" OR "structural change\*" OR "brain structure" OR "cortical thickness" OR "grey matter volume" OR "grey matter density" OR "gray matter volume" OR "gray matter density" OR "hippocampal volume\*" OR "brain atrophy" OR "brain activit\*" OR "neural activit\*" OR "cognitive function\*" OR "functional connectivity" OR "white matter integrity" OR "white matter structure" OR "white matter tract\*" OR "fractional anisotropy" OR "radial diffusivity" OR "axial diffusivity" OR "neural connectivity" OR "brain metabolism" OR "metabolic connectivity" OR "cerebral glucose metabolism" OR "cognitive performance\*" OR "cognition" OR "neuropsychological data" OR "cognitive functioning" OR "mental health" OR "executive function\*" OR "cognitive abilit\*" OR "mini-mental state examination" OR "MMSE" OR "cognitive reserve" OR "brain reserve")) OR (AB("brain structural change\*" OR "structural brain change\*" OR "structural change\*" OR "brain structure" OR "cortical thickness" OR "grey matter volume" OR "grey matter density" OR "gray matter volume" OR "gray matter density" OR "hippocampal volume\*" OR "brain atrophy" OR "brain activit\*" OR "neural activit\*" OR "cognitive function\*" OR "functional connectivity" OR "white matter integrity" OR "white matter structure" OR "white matter tract\*" OR "fractional anisotropy" OR "radial diffusivity" OR "axial diffusivity" OR "neural connectivity" OR "brain metabolism" OR "metabolic connectivity" OR "cerebral glucose metabolism" OR "cognitive performance\*" OR "cognition" OR "neuropsychological data" OR "cognitive functioning" OR "mental health" OR "executive function\*" OR "cognitive abilit\*" OR "mini-mental state examination" OR "MMSE" OR "cognitive reserve" OR "brain reserve")) OR (SU("brain structural change\*" OR "structural brain change\*" OR "structural change\*" OR "brain structure" OR "cortical thickness" OR "grey matter volume" OR "grey matter density" OR "gray matter



volume" OR "gray matter density" OR "hippocampal volume\*" OR "brain atrophy" OR "brain activit\*" OR "neural activit\*" OR "cognitive function\*" OR "functional connectivity" OR "white matter integrity" OR "white matter structure" OR "white matter tract\*" OR "fractional anisotropy" OR "radial diffusivity" OR "axial diffusivity" OR "neural connectivity" OR "brain metabolism" OR "metabolic connectivity" OR "cerebral glucose metabolism" OR "cognitive performance\*" OR "cognition" OR "neuropsychological data" OR "cognitive functioning" OR "mental health" OR "executive function\*" OR "cognitive abilit\*" OR "mini-mental state examination" OR "MMSE" OR "cognitive reserve" OR "brain reserve")) AND ((TI("Alzheimer's disease" OR "AD" OR "Alzheimer" OR "probable AD" OR "Alzheimer's dementia" OR "Alzheimer dementia" OR "AD dementia" OR "AD-dementia" OR "dementia due to AD" OR "mild cognitive impairment" OR "MCI" OR "aMCI" OR "a-MCI" OR "MCI due to AD" OR "subjective cognitive decline" OR "SCD" OR "subjective memory impairment" OR "cognitive complaint\*" OR "cognitive concern\*" OR "memory complaint\*" OR "memory concern\*")) OR (AB("Alzheimer's disease" OR "AD" OR "Alzheimer" OR "probable AD" OR "Alzheimer's dementia" OR "Alzheimer dementia" OR "AD dementia" OR "AD-dementia" OR "dementia due to AD" OR "mild cognitive impairment" OR "MCI" OR "aMCI" OR "a-MCI" OR "MCI due to AD" OR "subjective cognitive decline" OR "SCD" OR "subjective memory impairment" OR "cognitive complaint\*" OR "cognitive concern\*" OR "memory complaint\*" OR "memory concern\*")) OR (SU("Alzheimer's disease" OR "AD" OR "Alzheimer" OR "probable AD" OR "Alzheimer's dementia" OR "Alzheimer dementia" OR "AD dementia" OR "AD-dementia" OR "dementia due to AD" OR "mild cognitive impairment" OR "MCI" OR "aMCI" OR "a-MCI" OR "MCI due to AD" OR "subjective cognitive decline" OR "SCD" OR "subjective memory impairment" OR "cognitive complaint\*" OR "cognitive concern\*" OR "memory complaint\*" OR "memory concern\*"))))

Refined by: LANGUAGE (English) and AGE ('aged: 65 yrs & older' or 'very old: 85 yrs & older')



## Appendix 2: Summary of included studies

The papers are listed in alphabetical order.

Abbreviations used in the table: AC: Active Control group; ACC: Anterior Cingulated Cortex; AD: Alzheimer's disease; ADAS-Cog: Alzheimer's Disease Assessment Scale - Cognitive subscale; ARS: Auditory Reading Span; ANT: Attention Network Test; BFT: Benson Figure Test; BL: Bilinguals; BNT: Boston Naming Test; CERAD: Consortium to Establish a Registry for Alzheimer's Disease; CT: Computerized Tomography; D-KEFS: Delis-Kaplan Executive Function System; DTI: Diffusion Tensor Imaging; EF: Executive Functions; FUCAS: Functional Cognitive Assessment Scale; GM: Gray Matter; IFG: Inferior Frontal Gyrus; LAN: Language; LASSI-L: Loewenstein-Acevedo Scales for Semantic Interference and Learning; LI: Language Intervention group; MCI: Mild Cognitive Impairment; MMSE: Mini-Mental State Examination; ML: Monolinguals; MRI: Magnetic Resonance Imaging; PC: Passive Control group; PET: Positron Emission Tomography; RAVLT: Rey Auditory Verbal Learning Test; RBMT: Rivermead Behavioural Memory Test; ROCF: Rey-Osterrieth Complex Figure; SCD: Subjective Cognitive Decline; SES: Socioeconomic Status; ST: Simon Task; TEA: test of Everyday Attention; TMT: Trail Making Test; VSA: Visuospatial Ability; WM: Working Memory; WMS: Wechsler Memory Scale; \*\* High prevalence of multilingualism in the sample; <sup>a</sup> The cognitive tests used to assess the cognitive domains under investigation were not reported in the study; <sup>b</sup> The Clock Drawing test is used as a measure of EF, VSA, and episodic memory (see Kim et al. 2018)

| First author, year    | Intervention/comparator (group comparison type)  | Clinical group  | Outcome   | Confounds  | Main findings  |
|-----------------------|--|---|---|--|--|
| Ballarini et al. 2023 | Lifelong multilingualism<br>•Lifelong BL vs lifelong ML<br>•BL vs ML at three life stages: early, middle, late | •Cognitively healthy adults without SCD<br>•SCD<br>•Cognitively healthy adults at familial risk of AD | Domain-specific cognition (learning and memory, WM, EF, VSA, LAN) <sup>a</sup><br>GM volume<br>•MRI | •Years of education<br>•Physical activity<br>•SES<br>•Intelligence | •Significantly better performance on learning and memory, WM, EF, LAN in BL in early life<br>•Significantly better performance on learning and memory in BL in middle life<br>•No significant differences on GM volume between language groups |

| First author, year | Intervention/comparator (group comparison type) | Clinical group | Outcome  | Confounds                                  | Main findings  |
|--------------------|---|----------------|--|--|--|
| Calvo et al. 2023  | Lifelong multilingualism (BL vs ML)             | MCI due to AD  | GM density<br>•MRI<br>General cognition<br>•MMSE   | •Years of education<br>•Immigration status | •More significant GM loss in frontal and parietal areas, dorsal ACC and IFG pars orbitalis in BL<br>•No significant differences in MMSE score  |
| Clare et al. 2014  | Lifelong multilingualism (BL vs ML)             | AD dementia    | Domain-specific cognition (EF, WM)<br>•D-KEFS<br>•WMS<br>•Keep Track<br>•TEA<br>•Go-No Go<br>•ST<br>•Stroop task | •Years of education<br>•SES                | •Significantly lower MMSE scores in BL at the time of diagnosis<br>•No significant language-group differences on cognitive performance, except for better performance on category switching (D-KEFS subtest) in ML |



| First author, year    | Intervention/comparator (group comparison type) | Clinical group   | Outcome  | Confounds  | Main findings  |
|-----------------------|---|--|--|--|--|
| Costumero et al. 2020 | Lifelong multilingualism (BL vs ML)             | amnesic MCI  | Domain-specific cognition (LAN, WM, episodic Memory, EF, VSA)<br>•BNT<br>•Word acquisition and recall<br>•Remote memory test<br>•Clock-drawing test<br>GM volume<br>•MRI | Years of education   | <ul style="list-style-type: none"> <li>•No significant language-group differences at baseline but faster cognitive decline in ML in longitudinal analyses</li> <li>•More significant GM loss in BL at baseline but slower volume loss in longitudinal analyses</li> </ul>  |
| Duncan et al. 2017    | Lifelong multilingualism (BL** vs ML)           | <ul style="list-style-type: none"> <li>•AD dementia</li> <li>•Amnesic MCI</li> </ul> | GM density and cortical thickness<br>•MRI  | <ul style="list-style-type: none"> <li>•Years of education</li> <li>•Immigration status</li> </ul> | <ul style="list-style-type: none"> <li>•Greater cortical thickness in (language) control network structures, including IFG, pre-frontal cortex, and cerebellum, and greater GM density in hippocampus in MCI-BL but opposite trend in AD-BL</li> <li>•Positive associations between (language) control network structures and episodic memory in BL</li> </ul> |

| First author, year | Intervention/comparator (group comparison type) | Clinical group   | Outcome   | Confounds  | Main findings   |
|--------------------|---|--|---|--|---|
| Kowoll et al. 2015 | Lifelong multilingualism (BL** vs ML)           | <ul style="list-style-type: none"> <li>•AD dementia</li> <li>•MCI</li> </ul>           | General and domain-specific cognition (verbal abilities, WM, EF)<br><ul style="list-style-type: none"> <li>•MMSE</li> <li>•TMS</li> <li>•WMS</li> </ul>   | <ul style="list-style-type: none"> <li>•Years of education</li> <li>•Immigration status</li> </ul> | No significant differences between language-group   |
| Kowoll et al. 2016 | Lifelong multilingualism (BL** vs ML)           | <ul style="list-style-type: none"> <li>•AD dementia, MCI (grouped together)</li> </ul> | Cerebral glucose metabolism<br><ul style="list-style-type: none"> <li>•Fluorodeoxy-glucose PET</li> </ul> General and domain-specific cognition (verbal abilities, WM, EF)<br><ul style="list-style-type: none"> <li>•MMSE</li> <li>•TMS</li> <li>•WMS</li> </ul> | <ul style="list-style-type: none"> <li>•Years of education</li> <li>•Immigration status</li> </ul> | <ul style="list-style-type: none"> <li>•Lower values of glucose uptake (lower metabolic activity) in BL in frontal, temporal, parietal cortices, and left cerebellum</li> <li>•BL and ML did not differ on cognitive performance</li> </ul> |



| First author, year      | Intervention/comparator (group comparison type) | Clinical group | Outcome   | Confounds          | Main findings   |
|-------------------------|---|----------------|---|--------------------|---|
| Marin-Marin et al. 2020 | Lifelong multilingualism (BL vs ML)             | MCI            | White matter structural integrity<br>•DTI<br>Domain-specific cognition (LAN, WM, episodic Memory, EF, VSA)<br>•BNT<br>•Word list acquisition and recall<br>•Fluency<br>•Clock-drawing test <sup>b</sup> | Years of education | <ul style="list-style-type: none"> <li>•In BL, lower white matter integrity in tracts related to episodic memory and higher white matter integrity in tracts adjacent to the bilingual language network</li> <li>•No significant language-group differences on cognitive performance</li> </ul> |



| First author, year      | Intervention/comparator (group comparison type) | Clinical group | Outcome  | Confounds          | Main findings  |
|-------------------------|---|----------------|--|--------------------|--|
| Marin-Marin et al. 2021 | Lifelong multilingualism (BL vs ML)             | MCI            | Cerebral resting-state functional connectivity<br>•MRI<br>Domain-specific cognition (LAN, WM, episodic Memory, EF, VSA)<br>•BNT<br>•Word list acquisition and recall<br>•Fluency<br>•Clock-drawing test <sup>b</sup> | Years of education | •Significantly greater connectivity in the language network in BL<br>•No significant language-group differences on cognitive performance |

| First author, year | Intervention/comparator (group comparison type) | Clinical group | Outcome   | Confounds  | Main findings   |
|--------------------|---|----------------|---|--|---|
| Perani et al. 2017 | Lifelong multilingualism (BL vs ML)             | AD dementia    | Cerebral resting-state metabolic activity and connectivity<br>•Fluorodeoxy-glucose PET Domain-specific cognition (LAN, attention, verbal short-term and long-term memory, VSA) <sup>a</sup> | Years of education   | <ul style="list-style-type: none"> <li>•Significant hypometabolism in the frontal, temporal and parietal regions of the brain (i.e., left IFG), the ACC, and (right) putamen and cerebellum</li> <li>•Significant increase in anterior-posterior metabolic connectivity in BL</li> <li>•No significant differences between BL and ML on language and attention</li> </ul> |
| Raji et al. 2020   | Lifelong multilingualism (BL vs ML)             | AD dementia    | Brain volume<br>•MRI  | <ul style="list-style-type: none"> <li>•Years of education</li> <li>•Immigration status</li> </ul> | <ul style="list-style-type: none"> <li>•Larger brain volumes in BL when matched on cognitive performance with ML</li> <li>•Volume in thalamus, frontal lobes, temporal lobes and whole brain volume correlated with MMSE score</li> </ul>   |

| First author, year    | Intervention/comparator (group comparison type) | Clinical group | Outcome  | Confounds                                   | Main findings  |
|-----------------------|---|----------------|--|---|--|
| Rosselli et al. 2019  | Lifelong multilingualism (BL vs ML)             | aMCI           | Domain-specific cognition (verbal and nonverbal memory)<br>•LASSI-L<br>•BFT<br>Brain volume<br>•MRI                  | •Years of education<br>•Immigration status  | •Scores on LASSI-L measures related to inhibitory control were significantly higher in BL than ML<br>•Scores on LASSI-L measures related to inhibitory control were significantly correlated with volumetric reductions in the hippocampus in BL and ML and entorhinal cortex in BL  |
| Sala et al. 2021      | Lifelong multilingualism (BL** vs ML)           | AD dementia    | Cerebral resting-state metabolic activity and connectivity<br>•Fluorodeoxy-glucose PET<br>General cognition<br>•MMSE | Years of education                          | •Significant hypometabolism in the left IFG, left superior middle and inferior temporal gyrus, insula and ACC<br>•Significant increase in connectivity in the language and executive control network in BL<br>•Higher degree of bilingualism was related to greater hypometabolism and increased connectivity<br>•No significant difference in cognition between BL and ML |
| Schweizer et al. 2012 | Lifelong multilingualism (BL vs ML)             | AD dementia    | Brain atrophy<br>•CT   | •Years of education<br>•Occupational status | Greater brain atrophy in medial-temporal lobes in BL when matched with ML on cognitive performance   |

| First author, year | Intervention/comparator (group comparison type) | Clinical group   | Outcome  | Confounds   | Main findings   |
|--------------------|---|--|--|---|---|
| Torres et al. 2021 | Lifelong multilingualism (BL vs ML)             | <ul style="list-style-type: none"> <li>•MCI</li> <li>•AD dementia</li> </ul> | GM volume<br><ul style="list-style-type: none"> <li>•MRI</li> </ul> Domain-specific cognition (EF)<br><ul style="list-style-type: none"> <li>•Digit Span Backwards</li> <li>•TMT</li> <li>•Stroop task</li> <li>•Category fluency</li> </ul>       | <ul style="list-style-type: none"> <li>•Years of education</li> <li>•Occupational status</li> </ul> | <ul style="list-style-type: none"> <li>•Greater GM volume in regions involved in language processing and EF in BL, specifically IFG in MCI and AD-BL, and orbitofrontal cortices in AD-BL</li> <li>•Reduced Stroop interference in BL, while ML outperformed BL in Digit Span backwards and category fluency</li> </ul> |
| Tikga et al. 2019  | Later-life language learning (LI vs PC)         | MCI  | General cognition and domain-specific cognition (verbal learning, memory, attention, EF, VSA)<br><ul style="list-style-type: none"> <li>•MMSE</li> <li>•FUCAS</li> <li>•TEA</li> <li>•RAVLT</li> <li>•RBMT</li> <li>•ROCF</li> <li>•TMT</li> </ul> | Years of education  | <ul style="list-style-type: none"> <li>•LI performed significantly better than PC on MMSE, RAVLT, ROCF, and FUCAS at pre-intervention</li> <li>•LI performed significantly better than PC on RAVLT and RBMT from pre- to post-intervention</li> </ul>   |





| First author, year | Intervention/comparator (group comparison type) | Clinical group | Outcome   | Confounds          | Main findings  |
|--------------------|---|----------------|---|--------------------|--|
| Voits et al. 2024  | Lifelong multilingualism (BL as a continuum)    | MCI due to AD  | Hippocampal volume<br>•MRI<br>Domain-specific cognition (episodic memory)<br>•CERAD Word List Memory Task           | n/a                | <ul style="list-style-type: none"> <li>•Greater hippocampal volume with active but unbalanced use of two languages (mid-range language entropy scores)</li> <li>•No significant association of language entropy with memory and no significant differences between language groups</li> </ul>  |
| Wong et al. 2019   | Later-life language learning (LI vs AC vs PC)   | MCI            | General cognition and domain-specific cognition (attention, WM)<br>•ADAS-Cog<br>•ARS<br>•ST<br>•WMS<br>•BNT<br>•ANT | Years of Education | <ul style="list-style-type: none"> <li>•No significant differences between groups at pre-test</li> <li>•ADAS-Cog, ANT, and WMS (digit span backwards) improved significantly from pre- to post-test and BNT from post-test to follow-up independent of group</li> <li>•Significant improvement of LI on ADAS-Cog from pre- to post-test, with an effect size slightly larger, although not significant, compared to AC and PC</li> </ul> |

### Appendix 3: Summary of studies retrieved through additional search

The papers are listed in alphabetical order.

Abbreviations used in the table: AC: Active Control group; EF: Executive Functions; LI: Language Intervention group; MoCA: Montreal Cognitive Assessment; PC: Passive Control group; WM: Working Memory; \* The type of associative memory test was not specified in the study

| First author, year   | Intervention/comparator (group comparison type) | Outcome   | Confounds          | Main findings  |
|----------------------|---|---|--------------------|--|
| Berggren et al. 2020 | Later-life language learning (LI vs PC)         | Domain-specific cognition (WM, long-term associative memory*)<br>•N-back task                             | Years of education | <ul style="list-style-type: none"> <li>•No significant differences between the LI and the PC on cognitive performance</li> <li>•No significant effect of language intervention on cognition</li> </ul>   |
| Meltzer et al. 2023  | Later-life language learning (LI vs AC vs PC)   | Domain-specific cognition (EF, WM)<br>•N-back task<br>•Simon task<br>•Stroop Color-Word Interference task | Years of education | <ul style="list-style-type: none"> <li>•The AC showed significantly faster reaction times and outperformed both the LI and PC on on subtasks measuring EF and WM in the N-back task</li> <li>•Significant improvement of the AC on Simon task compared to the PC and LI</li> <li>•General improvement but no between-group differences on the Stroop Color-Word Interference task</li> </ul> |
| Valis et al. 2019    | Later-life language learning (LI vs PC)         | General cognition<br>•MoCA  | Years of education | <ul style="list-style-type: none"> <li>•No significant differences between the LI and the PC on cognitive performance</li> <li>•No significant effect of language intervention on cognition</li> </ul>   |

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