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# Bilingualism/Multilingualism to Protect Against Cognitive Decline in Alzheimer's Disease and Other Forms of Dementia: A Systematic Review

Kirsten L. May

*University of South Dakota*

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BILINGUALISM/MULTILINGUALISM TO PROTECT AGAINST COGNITIVE DECLINE  
IN ALZHEIMER'S DISEASE AND OTHER FORMS OF DEMENTIA:

A SYSTEMATIC REVIEW

BY

KIRSTEN MAY

A Thesis Submitted in Partial Fulfillment  
of the Requirements for the  
University Honors Program

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Department of Biology  
The University of South Dakota  
May 2020

The members of the Honors Thesis Committee appointed  
to examine the thesis of Kirsten May  
find it satisfactory and recommend that it be accepted.

---

Elizabeth K. Hanson, Ph.D., CCC-SLP

Associate Professor of Communication Sciences and Disorders

Director of the Committee

---

Joyce Keifer, Ph.D.

Professor of Basic Biomedical Sciences

---

Angela Helmer, Ph.D.

Professor of Modern Languages and Linguistics

## **Abstract**

Bilingualism/multilingualism to protect against cognitive decline in Alzheimer's disease and other forms of dementia: A systematic review

Kirsten May

Director: Elizabeth K. Hanson, PhD., CCC-SLP

Given a growing incidence of Alzheimer's disease and lack of treatments, prevention is a popular topic in both research literature (Angevaren et al., 2008; Orrell & Sahakian, 1995) and in news articles (Iacono et al., 2009). A cognitive reserve is a skill that improves cognitive functioning in executive controls. Bilingualism is believed to be a practice that increases cognitive reserve, which could delay the onset of Alzheimer's disease.

The purpose of this project was to analyze the possibility that bilingualism or multilingualism could create a cognitive reserve to delay the onset of Alzheimer's disease and other dementia-related diseases. This systematic review asks the question: Can bilingualism and multilingualism function as a protective mechanism and create a cognitive reserve to delay the onset and progression of Alzheimer's disease and other dementia-related diseases?

The PRISMA approach was used and evidence was gathered from the databases of PubMed and Web of Science. Evidence was screened for inclusion and appraised for quality by following similar criteria to the study from Mukadam and colleagues (2017). The results of the studies were summarized through tables and comparisons. Neural reserve and cognitive reserve studies investigating both structural and behavioral differences found greater statistical differences for bilinguals and multilinguals, showing a potential benefit of language usage towards preventing Alzheimer's disease and other dementia-related disease. Studies only

investigating cognitive reserve did not find as overwhelming evidence for multiple language use to delay such diseases. I hope to clarify the debatable role of multiple languages to create a cognitive reserve that may delay Alzheimer's disease and other forms of dementia.

**KEYWORDS:** Bilingual, Alzheimer's Disease, Cognitive Reserve

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## CHAPTER ONE

### Introduction to Dementia Related Diseases

#### What is Alzheimer's Disease?

Alzheimer's disease is defined as a type of irreversible and progressive dementia with decline in two or more of the cognitive domains: memory, language, executive and visuospatial function, personality and behavior (Weller, 2018). These symptoms often interfere with the activities of daily living. When the symptoms do not interfere with daily functions, it is termed to be mild cognitive impairment (Albert et al., 2011). Alzheimer's disease is the most common type of dementia, accounting for up to 80% of dementia-related cases (Prince, 2015). The prevalence of Alzheimer's disease within the United States was reported to be 46.8 million people in 2015, and it is estimated to nearly triple by the year 2050 (Prince, 2015). This continuously increasing incidence of Alzheimer's disease puts a strain on social and healthcare systems.

#### Prevention and Treatment

The standards of diagnosis have changed in the last decade to better discriminate amongst different dementia-related diseases (McKhann et al., 2011). The most current pathological criteria for Alzheimer's disease diagnosis consist of two main measures: increased levels of amyloid-beta ( $A\beta$ ) peptide and increased levels of hyperphosphorylated tau (p-tau) proteins (Dubois et al., 2016). These molecules are associated respectively with the characteristic brain pathology of plaques and tangles in Alzheimer's disease. There are two stages of diagnosis: preclinical and clinical. The preclinical stage occurs prior to symptoms for clinical Alzheimer's disease

diagnosis. However, pathological signs can begin up to 20 years before full progression to clinical Alzheimer's disease (Dubois et al., 2016). Thus, treatment and prevention has shifted to being aimed at the preclinical stages of Alzheimer's disease.

Currently, there is no successful cure for Alzheimer's disease. It is an area of great interest in research; however, the disease is complicated and there is much research still to be done within the field. Preventative factors may show promise in delaying or slowing the progression of Alzheimer's disease. These factors range from exercise, diet, cognitive training, maintaining strong social connections, to managing vascular and metabolic risk factors (Ngandu et al., 2015). Genetic factors such as a variant in the APP gene may also provide a protective benefit against Alzheimer's disease (Jonsson et al., 2012). In the interest of this systematic review, cognitive training is characterized by the regular usage of a more than one language.

## CHAPTER TWO

### Introduction to Cognitive Reserve

#### What is Cognitive Reserve?

Cognitive Reserve is defined as a modulator between neuropathological damage and clinical outcomes such as those associated with Alzheimer's disease (Stern, 2006). There are several hypotheses behind the mechanism of cognitive reserve. One is that individuals with larger brains have more synapses and neurons to lose before brain damage reaches a clinical diagnosis (Katzman et al., 1988). Another hypothesis, termed "brain reserve capacity," states that brain reserve is fixed, and once depletion has surpassed a certain threshold, clinical or functional deficits result (Satz, 1993). However, a more probable hypothesis is that the brain can cope with brain damage by using compensatory networks, or alternative networks unaffected by damage that are not normally utilized for that specific processing task in healthy brains (Stern, 2006). The first two hypotheses are more quantitative in nature, whereas the cognitive reserve idea is more descriptive and individualized in the compensatory mechanisms utilized as suggested by Stern and colleagues (2006). The individualized nature of cognitive reserve makes it harder to quantify for research. Thus, there is great variability in the methods to measure cognitive reserve and its association to Alzheimer's disease and other dementia-related diseases.

#### List of Possible Cognitive Reserves

There are a variety of cognitively stimulating factors that can provide cognitive reserve. One interesting activity that has shown evidence for cognitive reserve is aerobic exercise which increases respiratory capacity as well as brain function (Angevaren et al., 2008). Education and

sustained mental activity are two strong predictors of delayed onset of dementia, and they likely do so by providing cognitive reserve (Orrell & Sahakian, 1995). To go further, any activities that challenge an individual mentally provide good opportunity for cognitive reserve. These activities range from brain game, activities that stimulate working memory, or, in the case of the focus of this paper, regular usage of another language (Gold, 2015). These factors influence compensatory networks contributing to cognitive reserve.

## CHAPTER THREE

### Introduction to Neural Reserve

#### What is Neural Reserve?

Neural reserve is defined as the difference found between the observed cognitive functioning and the expected reduced functioning associated with pathological Alzheimer's disease (Luk et al., 2010). This associated capacity for resilience relies more on anatomic indices, in comparison to cognitive reserve which relies more heavily on functional indices. These anatomic indices include brain size, gray matter volume and density, synaptic count and dendritic branching (Stern, 2012). It should be mentioned that while neural and cognitive reserve are similar and likely associated with each other; they are separate from one another and not interchangeable.

#### Language and Memory Areas of the Brain

Several areas of the brain are important in the production of language and memory and, thus, are areas of focus for identifying neural reserve. Wernicke's area, located in the superior temporal gyrus and the posterior Sylvian fissure, is associated with speech comprehension (Galaburda & Sanides, 1980). Broca's area, located in the pars triangularis and the opercularis of the inferior frontal gyrus, is associated with the production of speech (Aboitiz & García, 1997). Working memory is the short-term memory of sensory information before either long-term storage or discarding of the information and is broadly distributed across the brain (Goldman-Rakic, 1987). Language also tends to be localized in the left hemisphere.

## CHAPTER FOUR

### Methods

#### Identifying the Research Question

The primary question of this scoping review was: Can bilingualism or multilingualism function as a protective mechanism against the onset and progression of Alzheimer's disease and other dementia-related diseases?

#### Finding Relevant Studies

##### *Search Strategy:*

Evidence was collected from April 2019 through December 2019. Academic Search Premier was the first database used with the search terms “bilingual” and “Alzheimer's disease” yielding 717 results. After looking at the first 50 results, more specific and inclusive search terms were needed to continue. The search continued on April 17<sup>th</sup>, 2019. Evidence was gathered from the databases PubMed and Web of Science. The search terms were “bilingual” or “language” and “dementia”, “AD”, “Alzheimer\*” or “cognit\*”. The search yielded 183,104 and 98,489 results for Web of Science and PubMed respectively. Figure 1 and Figure 2 illustrate how this search proved to be far too broad. During this process, a systematic review and meta-analysis by Mukadam et al. (2017) was found that encompassed the aim of the research question. Therefore, the protocol used

by Mukadam and colleagues was replicated. Articles were narrowed through criteria limiting the articles to be in English and have a publishing date after 2016.

## Figure 1

### *Initial Search Results in Web of Science*

The screenshot shows the Web of Science interface with the following details:

- Search Results:** 664,789 (from Web of Science Core Collection)
- Search Query:** "bilingual" OR "language" AND "dementia", "AD", "Alzheimer" OR "cognit"
- Sort by:** Relevance
- Filters:**
  - Highly Cited in Field (4,800)
  - Hot Papers in Field (90)
  - Open Access (166,847)
  - Associated Data (5,508)
- Publication Years:** Filtered to 2016-2019
- Top Results:**
  - Primary progressive aphasia: Diagnosis, varieties, evolution**  
By: Kertesz, A; Davidson, W; McCabe, P; et al.  
JOURNAL OF THE INTERNATIONAL NEUROPSYCHOLOGICAL SOCIETY Volume: 9 Issue: 5 Pages: 710-719  
Published: JUL 2003
  - Self-reported written Japanese language ability and risk for any dementia, Alzheimer's disease (AD) and vascular dementia (VD): The Honolulu Asia aging study (HAAS)**  
By: Arani, K. N.; Gibbons, L.; White, L.; et al.  
Conference: Western Regional Meeting of the American-Federation-for-Medical-Research Location: Carmel, CA  
Date: JAN 30-FEB 02, 2008  
Sponsor(s): Amer Federat Med Res  
JOURNAL OF INVESTIGATIVE MEDICINE Volume: 56 Issue: 1 Pages: 206-206 Meeting Abstract: 309  
Published: JAN 2008
  - Severity of Alzheimer's disease and language features in picture descriptions**  
By: Kave, Gitit; Dassa, Ayelet  
APHASIOLOGY Volume: 32 Issue: 1 Special Issue: SI Pages: 27-40  
Published: 2018

*Note.* Initial search results yielded 664,789 hits.

## Figure 2

### *Initial Search Results in PubMed*

The screenshot shows the PubMed interface with the following details:

- Search Query:** "bilingual" OR "language" AND "dementia", "AD", "Alzheimer" OR "cognit"
- Format:** Summary
- Sort by:** Best Match
- Filters:**
  - Publication date from 2016/11/23 to 2019/12/31
- Search Results (1 to 20 of 98489 items):**
  - Physical Activity and Alzheimer's Disease: A Systematic Review.**  
Stephen R. Hongisto K, Solomon A, Lonnroos E.  
J Gerontol A Biol Sci Med Sci. 2017 Jun 1;72(6):733-739. doi: 10.1093/geronl/gw251. Review.  
PMID: 29049634
  - Molecular Pathogenesis of Alzheimer's Disease: An Update.**  
Sanabria-Castro A, Alvarado-Echeverria I, Monge-Bonilla C.  
Ann Neurol. 2017 May;24(1):68-84. doi: 10.1159/00046422. Epub 2017 Apr 21. Review.  
PMID: 28588356 Free PMC Article
  - Rivastigmine: the advantages of dual inhibition of acetylcholinesterase and butyrylcholinesterase and its role in subcortical vascular dementia and Parkinson's disease dementia.**  
Kandiah N, Pal MC, Senanarong V, Looi I, Ampil E, Park KW, Karanam AK, Christopher S.  
Clin Interv Aging. 2017 Apr 18;12:697-707. doi: 10.2147/CIA.S129145. eCollection 2017. Review.  
PMID: 28458525 Free PMC Article
  - Language and communication non-pharmacological interventions in patients with Alzheimer's disease: a systematic review. Communication intervention in Alzheimer.**  
Morello ANDC, Lima TM, Brandão L.  
Dement Neuropsychol. 2017 Jul-Sep;11(3):227-241. doi: 10.1590/1980-67642016dn11-030004.  
PMID: 29213519 Free PMC Article

*Note.* Initial search results yielded 98,489 hits.

**Table 1**

*Databases, Search Terms, and Results*

<u>Databases Searched</u>	<u>Search Terms</u>	<u>Hits</u>	<u>Used Hits</u>	<u>Article</u>
PubMed	“bilingual” or “language” and “dementia”, “AD”, “Alzheimer*” or “cognit*”	98489	8	Duncan et al (2018) Estanga et al. (2017) Gollan et al. (2017) Klein et al. (2016) Klimova et al. (2017) Kowoll et al. (2016) Lombardi et al. (2018) Perani et al. (2017)
Web of Science	“bilingual” or “language” and “dementia”, “AD”, “Alzheimer*” or “cognit*”	183104	7	Alvarez & Rodriguez (2016) Duncan et al (2018) Estanga et al. (2017) Gollan et al. (2017) Klimova et al. (2017) Lombardi et al. (2018) Perani et al (2017)

*Note.* Studies were greatly narrowed from the preliminary search to the final used hits.

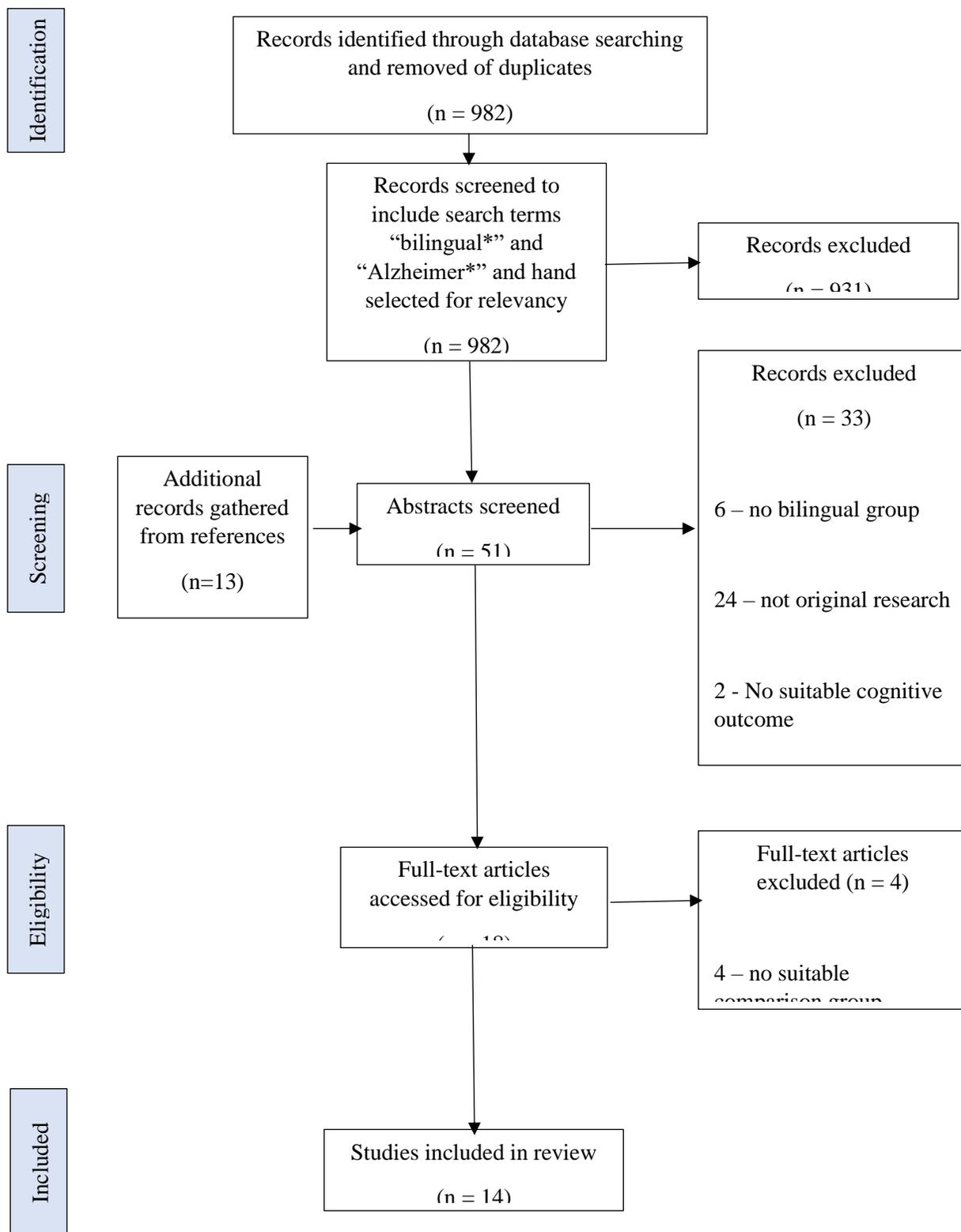
## Selecting the Studies

### *Searches and Inclusion of Papers:*

From there, the results were transferred to Endnote where articles were narrowed with inclusion and exclusion criteria as specified in Mukadam et al. (2017) as well as searched for “Alzheimer\*” bringing the search down to nine articles. Reference sections from the nine included articles were reviewed, and an additional thirteen articles were identified to be screened with inclusion and exclusion criteria. This was a procedure that I replicated from Mukadam and

colleagues (2017). As a result, four more articles were included in this systematic review. The PRISMA, or Preferred Reporting Items for Systematic Review and Meta-Analyses, approach was used while selecting articles. This is a method that shows the flow of information through the different stages of systematic reviews and meta-analyses with the number of articles identified, number of articles included and excluded, and the reasoning behind such. Figure 3 shows the process of inclusion and exclusion up to the arrival at the final fourteen studies for inclusion and appraisal.

Figure 3

*PRISMA Diagram Displaying Results and Included Studies*

*Inclusion criteria:*

- Group speaking more than one language and a group that did not for comparison
- Participants without pre-existing neurological disorders were assessed for cognitive function
- Participants had a diagnosis or received a quantitative cognitive outcome for cognition, dementia, or mild cognitive impairment

*Exclusion Criteria:*

- Abstracts and letters
- Comparisons between bilinguals and multilinguals without including the monolingual control group

*Quality Assessment:*

Each source was assessed for quality using the eight-point Newcastle-Ottawa scale for non-randomized studies (Wells et al., 2013). Points were awarded for inclusion of criteria. The criteria of this scale asked the following:

- Was the cohort an accurate representation of the defined population?
- Was the exposure to a second language well-defined and objectively measured?
- Was the outcome objectively measured and valid?
- Were confounders accounted for?
- Were follow-up rates high (>70%)
- Was the time to follow-up long enough (>5 years)?

Sources received a higher quality score for specifying a definition of bilingualism or a language assessment, cognitive measures that were valid, reliable, and were adjusted for confounding variables such as “age, sex, education, vascular risk factors, and other potential confounders such as immigration and socioeconomic status” (Mukadam et al., 2017, p.46). Authors were not contacted for additional information as criteria to appraise studies was sufficient to make an accurate quality assessment. Breakdown of points awarded in the quality assessment are included in Table 2.

**Table 2**

**Newcastle-Ottawa Scale for Non-randomized Studies**

	<b>Score</b>
1. Cohort as representative of underlying population as possible.	1
2. Definition of bilingualism (one point for well-defined definition of bilingualism, another if objective measure of language ability).	2
3. Outcome measure is objective and valid. Ideally diagnosis should be made via structured assessment by trained people, valid scale or criteria for diagnosis.	1
4. Adjustment of results for confounders. One point for adjusting for age, sex, education and another point if it considered any of the following: immigration status/SES, vascular risk factor	2
5. At least 70% follow up rates	1
6. Length of follow up at least 5 years.	1
<b>Total</b>	<b>8</b>

Note. Supplementary Table from Mukadam et al. (2017)

## CHAPTER FIVE

### Results

Anatomical and physiological brain differences are measured as a proxy for neural reserve to test the hypothesis that bilingualism can delay cognitive decline. Additionally, functional differences were measured as a proxy for cognitive reserve through behavioral assessments. These studies ranged in differences in study methods, participant composition, and confounding variables. One study method measuring gray matter density through magnetic resonance imaging to identify areas of the brain with more intact structure. Gray matter is located primarily in the cortex and nuclei of the brain, and it is the site specific to brain synapses and activation. Another method utilized glucose uptake to measure the metabolic activity of different regions of the brain. Diffusion tensor imaging (DTI) was a method for one particular study to assess the integrity of myelinated axons, or brain pathways. Participant pools varied geographically, culturally, and economically which can have a significant impact on confounding variables that can lessen the validity of different studies. Table 3 highlights the important aspects of each study and appraises the articles with a quality score.

**Table 3**

*Appraisal of Neural and Cognitive Reserve Studies*

<u>Study</u>	<u>Study Type</u>	<u>Quality score</u>	<u>Setting and participants : country</u>	<u>Baseline differences</u>	<u>N</u>	<u>Number of years follow-up</u>	<u>Follow-up rate (%)</u>	<u>Definition of bilingualism: comparator groups</u>	<u>Procedure</u>	<u>What controlled for</u>	<u>Outcome</u>
Anderson, J. A. E., Grundy, J. G., De Frutos, J., Barker, R. M., Grady, C., & Bialystok, E. (2018). Effects of bilingualism on white matter integrity in older adults. <i>Neuroimage</i> , 167, 143-150. doi:10.1016/j.neuroimage.2017.11.038	Retrospective	2	Healthy older adults recruited from community; Canada	Monolinguals had better letter number switching scores and percent switching accuracy	61	NA	NA	Background questionnaire and telephone interview; monolingual	Diffusion tensor imaging, D-KEFS battery (Delis et al., 2001), demographic and IQ information (Shipley, 1940)	Verbal and Spatial IQ, age, education, Trail-Making-Task, Mini-Mental State Examination (MMSE), gender	Lifelong bilingualism causes greater axial diffusivity in left superior longitudinal fasciculus bilinguals (p<0.05**)
Borsa, V. M., Perani, D., Della Rosa, P. A., Videsott, G., Guidi, L., Weekes, B. S., Franceschini,	Retrospective	2	Selected twenty bilingual and twenty monolingual participants; Italy	Bilingual participants had a higher MMSE	40	NA	NA	Self-reported questionnaire and picture naming test; monolingual	Attention Network Task, structural MRI to determine effects of	Age, education, SES, GMV of extent of anterior cingulate	No significant difference on behavioral test of cognitive

R., & Abutalebi, J. (2018). Bilingualism and healthy aging: Aging effects and neural maintenance. <i>Neuropsychologia</i> , <i>111</i> , 51-61. doi:10.1016/j.neuropsychologia. 2018.01.012									aging on grey matter volume	cortex activation	control (ANT) and GMV; GMV in dorsal anterior cingulate cortex and second language usage predict cognitive control ( $p=0.035^{**}$ )
Del Maschio, N., Sulpizio, S., Gallo, F., Fedeli, D., Weekes, B. S., & Abutalebi, J. (2018). Neuroplasticity across the lifespan and aging effects in bilinguals and monolinguals. <i>Brain Cogn</i> , <i>125</i> , 118-126. doi:10.1016/j.ba	Retrospective	2	Healthy young adult and senior participants; China and Italy	No significant differences in age, education, and MMSE scores	88	NA	NA	Picture- naming task and translation task; older and young monolingual	GMV to determine neural reserve and response time on Flanker test	Total intracranial volume	Cognitive decline from GMV loss in executive control networks delayed in bilinguals ( $p<0.005^{**}$ )

ndc.2018.06.00

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Duncan, H. D., Nikelski, J., Pilon, R., Steffener, J., Chertkow, H., & Phillips, N. A. (2018). Structural brain differences between monolingual and multilingual patients with mild cognitive impairment and Alzheimer disease: Evidence for cognitive reserve. <i>Neuropsychologia</i> , <i>109</i> , 270- 282. doi:10.1016/j.neuropsychologia. 2017.12.036	Retrospective	4	Memory clinic patients diagnosed with mild cognitive impairment (MCI) or Alzheimer's disease (AD); Canada	Immigratio n status, age of acquisition, proficiency , and contextual use of language in bilingual group	94	NA	NA	Majority of life using at least two languages, criterion from Bialystok et al., 2007; monolingual	Compared cortical thickness and tissue density in language and cognitive control (LCC) brain areas with MRI scans.	Demograph ic variables, age, years of education, MMSE, time between neuropsych ological assessment and scan, and episodic memory	Increased brain matter in multilingua l MCI and AD patients (p < 0.026**), evidence of bilingualis m as cognitive reserve in AD patients (all p < 0.009*), correlation between episodic memory and LCC areas, no difference in non- immigrant patients
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Estanga, A., Eca-Torres, M., Ibanez, A., Izagirre, A., Villanua, J., Garcia-Sebastian, M., Gaspar, M. T. I., Otaegui-Arrazola, A., Iriondo, A., Clerigue, M., & Martinez-Lage, P. (2017). Beneficial effect of bilingualism on Alzheimer's disease CSF biomarkers and cognition. <i>Neurobiol Aging</i> , 50, 144-151. Retrieved from <a href="https://doi.org/10.1016/j.neurobiolaging.2016.10.013">Go to ISI://WOS:000396891600017</a>	Prospective	6	Healthy volunteers in GAP study aged 40 to 80 years; Spain	Bilinguals were more educated, had higher level occupations, and higher vocabulary scores on WAIS-III	278	3	91, 80 CSF donation	Semi structured interview and "Bilingual Language Profile" questionnaire; ability to communicate in at least 2 languages from spoken language with regular usage of both	Clinical and neuropsychological evaluation, APOE genotype, white matter hyperintensities, cerebrospinal fluid (CSF) analyses, Framingham index for cardiovascular disease risk	Gender, age, MMSE, APOE-4 carrier distribution, Framingham CVD index, Fazekas score and direct family history of AD	Early bilinguals had lower CSF t-tau levels ( $p = 0.019^{**}$ ), less preclinical AD stage 1, stage 2 and SNAP ( $p = 0.02^{**}$ ), and better performance on executive and visual-spatial functions (no significant differences)
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Kowoll, M. E., Degen, C., Gorenc, L., Kuntzelmann, A., Fellhauer, I., Giesel, F., Haberkorn, U., & Schroder, J. (2016). Bilingualism as a Contributor to Cognitive Reserve? Evidence from Cerebral Glucose Metabolism in Mild Cognitive Impairment and Alzheimer's Disease. <i>Front Psychiatry</i> , 7. Doi:10.3389/fps yt.2016.00062	Retrospective	3	People in memory clinic diagnosed with MCI or AD; Germany	Bilinguals had more years of education, were more likely to be immigrants and showed a higher proportion of AD pathology compared to MCI	30	NA	NA	Majority of life regularly using two languages, criterion from Bialystok et al., 2007; monolingual	Screened using physical and neuropsycholo gical tests, blood tests, and FDG- PET scans	Age, gender, years of education	Lower glucose uptake in bilinguals ( $p < 0.05^{**}$ ), bilingualis m contributes to cognitive reserve
Perani, D., Farsad, M., Ballarini, T., Lubian, F., Malpetti, M., Fracchetti, A., Magnani, G., March, A., & Abutalebi, J.	Retrospective	3	Patients from the San Raffaele Hospital in Milan and the Bozen Central Hospital in early disease	Visuospatia l short-term memory, verbal short-term, and long- term memory	85	NA	NA	Bilingual Aphasia Test (Paradis et al., 1987), percentage of daily use and exposure to each language in	Examined for differences in cognitive impairments, FDG-PET imaging	Education, age, sex, occupation, urban vs. rural dwelling	Less glucose metabolize d in bilingual patients ( $p < 0.05^{**}$ ) and better performanc

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(2017). The impact of bilingualism on brain reserve and metabolic connectivity in Alzheimer's dementia. <i>Proc Natl Acad Sci U S A</i> , 114(7), 1690-1695. Doi:10.1073/pnas.1610909114	stages of AD (<3 years); Italy	better in bilinguals	bilingual group; monolingual	e on memory tasks; bilingual subjects 5 years older
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Note. Quality assessment score from Newcastle-Ottawa scale (Wells et al., 2013). Point values explained in methods.

\*p = bilinguals significant for neural reserve

\*\*p = bilinguals significant for cognitive reserve

The purpose of Anderson et al. (2018) was to identify with diffusion tensor imaging differences in white matter integrity between bilingual and monolingual healthy, older adults, and if these difference in white matter integrity could provide evidence for bilingualism as a neural reserve. Diffusion tensor imaging was identified as a potential indicator for measuring neural reserve, as diffusion tensor imaging measures the integrity of neural pathways through quantifying myelination within axons. The myelin sheath is the protective covering on axons which increases the speed of nerve impulses. Myelinated axons are a large component of white matter. Three factors were tested to determine white matter integrity: axial diffusivity, radial diffusivity, and fractional anisotropy. The hypothesis was that bilingual participants would have greater white matter integrity in the corpus callosum, superior longitudinal fasciculi, and inferior fronto-occipial fasciculi.

Results from this study indicated that people who were bilingual showed greater axial diffusivity in the left superior longitudinal fasciculus. This region is important in connecting the pars opercularis (Broca's area) with the receptive language areas of Wernicke's area in the temporal lobes. This tract contributes to language production and learning. A second language may strengthen the left superior longitudinal fasciculus for neural reserve. With the greater myelination density in bilingual participants, the hypothesis that bilingual participants would have greater white matter integrity, and consequentially neural reserve, was confirmed. The two groups did not differ significantly for cognitive reserve which was measured with the Trail-Making-Task and Mini-Mental State Examination. No limitations were identified in the article.

The purpose of Borsa et al. (2018) was to identify the impact of bilingualism as a cognitive and neural reserve during the healthy aging process. Factors such as chronological age, gray matter volume, cognitive control scores from the Attentional Network Task (Fan et al., 2002), and language background variables were investigated. The bilateral inferior parietal lobule, bilateral inferior frontal gyrus, bilateral insula, bilateral caudate nuclei and dorsal anterior

cingulate cortex are brain structures specifically related to cognitive control. Of these, the anterior cingulate cortex was identified as a region-of-interest. The hypothesis was that there would be more significant decline in monolingual cognitive control than in bilingual speakers and that gray matter volume of the anterior cingulate cortex and performance on the cognitive control task would be positively correlated to measures of language background.

Results from this study indicated that there was no protective benefit in reference to total neural reserve, or mean gray matter volume, from the bilingual experience. Bilingual and monolingual seniors were equally as likely to lose gray matter volume. Additionally, performance on cognitive control tasks was not improved among bilingual participants. Monolingual participants showed a more extended, bilateral pattern of neural decline, whereas bilingual participants had better preservation within the right hemisphere. Two findings could provide evidence for a bilingual advantage. First, the bilingual experience may promote neural maintenance as seen by the preservation of certain neural structures. Second, while the dorsal anterior cingulate cortex was the only brain region unaffected by chronological age for both monolingual and bilingual groups, bilinguals showed greater integrity of the dorsal anterior cingulate cortex and cognitive control performance. Lastly, the increased daily exposure to a second language improved cognitive control performance.

The purpose of Del Maschio et al. (2018) was to investigate the association between bilingualism and neuroplastic changes in the executive control networks in both young and aging populations and determine executive control capabilities. Cognitive efficiency was assessed through the gray matter volume with magnetic resonance imaging (MRI) and response time performance on the Flanker task. The Flanker task is a common test administered in attention and conflict monitoring studies (Fan et al., 2005). The hypothesis was that lifelong bilingualism would serve as a protector from the normal aging process and contribute to more gray matter volume and better Flanker task performances.

Results from this study confirmed the original hypothesis that the environmental variable of lifelong usage of a second language promotes cognitive reserve in aging and lessens neural decline in senescence. This neuroplasticity was shown to begin at a relatively early age and continued into old age. Despite clear deterioration in gray matter volume across many brain regions important for executive functioning, senior bilinguals showed a reduction in age-related performance decline in the Flanker test due to greater neural reserve most likely from bilingualism-induced neuroplastic changes. The younger bilingual participants did not benefit in regard to executive control performance from increased gray matter volume. In summary, the study found that bilinguals showed a delay in age-related cognitive decline from gray matter volume loss in the executive control network. The strength of these results was reduced by a limitation from cultural differences between the bilingual participants from Hong Kong and the monolingual participants from Milan.

The purpose of Duncan et al. (2018) was to examine the differences in cortical thickness and tissue density among multilingual and monolingual Alzheimer's disease and mild cognitively impaired participants as a means to examine the protective role of using multiple languages. There were four ways in which this hypothesis was tested. First, cortical thickness in language and cognitive control regions, areas in the brain associated with executive function, language, and the control of language, was investigated. Second, neuroanatomical differences were examined in the disease related regions of the brain consisting of the hippocampus, parahippocampal gyrus, and rhinal sulcus involved in episodic memory. Third, cognitive reserve was tested for a relationship between the language and cognitive control brain areas and episodic memory. Lastly, the confounder of immigrant status was investigated by replicating the study with non-immigrant monolingual and multilingual mild cognitively impaired patients (Alladi et al., 2017; Duncan et al., 2018). Magnetic resonance imaging (MRI), neuropsychological assessments, and clinical

severity and cognitive functioning measures were gathered and statistically examined to investigate each hypothesis.

Results from this study indicated several important findings. First, people who were multilingual and had mild cognitive impairment and Alzheimer's disease displayed greater gray matter density and cortical thickness than their monolingual counterparts. Second, evidence for multilingualism acting as a cognitive reserve was observed in posterior parahippocampal gyri and the rhinal sulci. A thinner cortex with equivalent episodic memory performance demonstrated the ability of cognitive reserve to compensate for atrophy of brain areas involved in memory processing. Third, positive correlations were observed between areas of language processing and cognitive reserve and episodic memory scores suggesting the usage of compensatory, or alternative, networks for maintenance of memory functioning. Lastly, immigrant status was tested and did not prove to alter the validity of the study. Being a retrospective study, language history, such as age of acquisition and proficiency, and demographic information on participants was not available; this limited the study because it is important for the accuracy of baseline differences. Lastly, a larger sample size would have allowed a separation among monolinguals, bilinguals and multilinguals which would have provided better representation of the cognitive impact of Alzheimer's disease.

The purpose of Estanga et al. (2016) was to investigate the cognitive performance and cerebrospinal fluid Alzheimer's disease-biomarker differences among monolinguals, early bilinguals, and late bilinguals, if there are differences, and to investigate the role of bilingualism on associations between cerebrospinal fluid Alzheimer's disease-biomarkers, age and cognition. The bilingual participants were recruited from the Basque region of Spain which is unique in that Basque has no close resemblance to any other language and bilingual participants are lifelong users of two languages. The study incorporated clinical and neuropsychological evaluation, white matter hypersensitivities, APOE genotype testing, and cerebrospinal fluid analyses. The clinical

evaluation included medical history, medication, cognitive and behavioral symptoms, neurological evaluation, blood work, cardiovascular disease risk and family risk of dementia. The neuropsychological evaluation tested the cognitive domains of memory, attention and executive function, and visuoceptive and visuoconstructive function.

Results from this study were favorable towards intellectual achievements and brain reserve. This study was able to observe the favorable effect of bilingualism on cerebrospinal fluid total-tau levels, a decrease in cerebrospinal fluid Alzheimer's disease-biomarkers with increasing age among bilingual participants and the lower prevalence of preclinical Alzheimer's disease among early bilingual subjects. Thus, early bilingualism may provide for a brain structure that is more resistant to tau-pathology. Bilingual subjects showed better performance on working memory, task switching ability and visual-spatial abilities. The study was limited by an inability to factor for differences in environmental, genetic, nutritional or educational differences. Additionally, it is possible that there may have been bias from the "Bilingual Language Profile" questionnaire (<https://sites.la.utexas.edu/bilingual>) which was the tool to measure language abilities because the data were self-reported. And lastly, although the sample sizes across the three participant groups were statistically strong, the number of pre-clinical Alzheimer's disease patients was small. Overall, bilingualism was shown to contribute to cognitive reserve and improved executive and visuospatial functions.

The purpose of Kowoll et al. (2016) was to investigate the cerebral glucose metabolism differences in bilingual and monolingual patients with Alzheimer's disease and mild cognitive impairment through [<sup>18</sup>F]fluorodeoxyglucose positron emission tomography using a specific neuroimaging technique for detecting Alzheimer's disease related brain changes. The hypothesis was that there would be significantly more impairment of glucose uptake in bilingual participants with both monolingual and bilingual participants performing similarly on behavioral performance

tests. This is due to the cognitive reserve theory that states that individuals with higher cognitive reserve can better compensate for pathological brain atrophy.

Results from this study supported the hypothesis; bilingual mild cognitively impaired and Alzheimer's disease patients showed significantly lower glucose uptake in regions such as frontal cortices, temporoparietal area, and the left cerebellum. Within the gyrus frontalis inferior of the frontal cortex, Brodmann's area (BA) 9 in the right hemisphere was significant and is a region linked to working memory, visuospatial memory and planning. Within the right temporal gyrus, Brodmann's area (BA) 21 is a region linked to language and semantic memory processing. Within the right and left inferior parietal lobe or Wernicke's area of the supramarginal gyrus, BA 40 is linked to reading, meaning and phonology. Within the left gyrus frontalis inferior, BA 47 is involved in processing functions but not necessarily linguistic processes. There were no significant differences between monolingual and bilingual patients in neuropsychological performance. Overall, the study found that bilingualism likely contributes to neural reserve as both bilinguals and monolinguals exhibited similar cognitive impairment with the bilinguals compensating for more structural brain changes in areas associated with speech, language and Alzheimer's disease pathology.

The purpose of Perani et al. (2017) was to assess the role of bilingualism as a protective factor by assessing the cerebral resting-state metabolic-activity with connectivity analysis for bilingual and monolingual participants with Alzheimer's disease. They used [<sup>18</sup>F]fluorodeoxyglucose positron emission tomography to measure this cerebral resting-state metabolism which is an index of synaptic function and density. The literature from Pernecky et al. (2006) and Garibotto et al. (2008) suggests that individuals with Alzheimer's disease and mild cognitive impairment, higher education, and occupation demonstrated usage of compensatory mechanisms through severe hypometabolism in temporoparietal areas and increased metabolism in the dorsolateral prefrontal cortex. The hypothesis was that bilingualism would create

neurobiological effects that would work as a protective factor and contribute to neural reserve. The two regions, the executive control network and the default mode network, were two regions of primary interest.

Results from this study indicated that bilingualism could delay Alzheimer's disease through neural compensation and neural reserve. Evidence for neural compensation was observed from severe hypometabolism bilaterally in the temporoparietal associative cortices, posterior cingulum and posterior precuneus and within the left hemisphere for the regions of the temporal cortex and inferior frontal gyrus, insula, and anterior cingulate cortex. However, there was increased metabolism in the orbitofrontal, inferior frontal and cingulate cortex among bilingual participants. These results were not dependent upon education with bilingual participants having significantly fewer years of education. Increased activity in the anterior frontal network may provide bilinguals with neural compensation. Bilingual participants demonstrated increased metabolic connectivity in the cingulate cortex, the inferior frontal gyrus, the parietal operculum, the insula, and the caudate nucleus within the frontoparietal executive control network and right hemisphere, suggesting a compensatory mechanism from dysfunction in the language dominant, left hemisphere. The default mode network showed an increased connectivity pattern between main language control structures in bilingual subjects such as the posterior cingulum and subcortical structures, that were comprised of the thalamus and the caudate nucleus bilaterally, and the anterior cingulum. Bilinguals were on average five years older than their monolingual counterparts. In alignment with the cognitive reserve theory, bilinguals demonstrated more extensive cerebral hypometabolism and better performance on memory and visuospatial tasks.

Several studies approached the topic of bilingualism and multilingualism to delay Alzheimer's disease and other dementia-related diseases solely from the cognitive reserve perspective. Behavioral performance on tasks that demonstrate better cognitive abilities and more executive functioning are used as a proxy for cognitive reserve. The tests include the Mini-Mental

State Examination, verbal and numerical Stroop tasks, the Boston naming test, and the National Adult Reading Test to name a few. These tests measure inhibition control, working memory, general intelligence, cognitive impairment, memory, attention, executive function, semantic memory, etc. The studies had a range of prospective and retrospective studies, varying participant pool composition and size, and confounding variables. Table 4 lists these differences in study design and appraises them with a quality score.

**Table 4**

*Appraisal of Cognitive Reserve Studies*

<u>Study</u>	<u>Study Type</u>	<u>Quality score</u>	<u>Setting and participants : country</u>	<u>Baseline differences</u>	<u>N</u>	<u>Number of years follow-up</u>	<u>Follow-up rate (%)</u>	<u>Definition of bilingualism: comparator groups</u>	<u>Procedure</u>	<u>What controlled for</u>	<u>Outcome</u>
Alladi, S., Bak, T. H., Shailaja, M., Gollahalli, D., Rajan, A., Surampudi, B., Hornberger, M., Duggirala, V., Chaudhuri, J. R., & Kaul, S. (2017). Bilingualism delays the onset of behavioral but not aphasic forms of frontotemporal dementia. <i>Neuropsychologia</i> , 99, 207-212. doi:10.1016/j.neuropsychologia.2017.03.021	Retrospective	3	Frontotemporal dementia patients at specialist clinic in Hyderabad; India	Bilinguals were more often male, more literate, higher skilled workers, 3.3 years older	193	NA	NA	Reliable family member reported, ability to communicate in two or more languages with others of same language; monolingual	Mini-Mental State Examination (MMSE), Addenbrooke's Cognitive Examination -revised, Clinical Dementia Rating, Frontal Systems Behavior Scale, semantic battery test	Years of education, occupation, literacy, sex, rural/urban residence, family history of dementia	Bilingual behavioral frontotemporal dementia group delayed over 6 years (62.6) than monolingual group (56.5, p=0.006*)

Anton, E., Garcia, Y. F., Carreiras, M., & Dunabeitia, J. A. (2016). Does bilingualism shape inhibitory control in the elderly? <i>Journal of Memory and Language, 90</i> , 147-160. doi:10.1016/j.jml.2016.04.007	Retrospective	3	Participants recruited in Basque Country; Spain	No differences of education, MMSE, or any demographic factor	48	NA	NA	Self-rated proficiency and interview by native speaker; monolingual	Preformed verbal and numerical Stroop test in highly proficient and varying proficient bilinguals	Education, MMSE, immigrant status, origin, intelligence, language proficiency	No significant difference in bilingual and monolingual monitoring abilities or inhibitory control
Clare, L., Whitaker, C. J., Martyr, A., Martin-Forbes, P. A., Bastable, A. J., Pye, K. L., Quinn, C., Thomas, E. M., Gathercole, V. C. M., & Hindle, J. V. (2016). Executive control in older Welsh monolinguals and bilinguals. <i>Journal of Cognitive Psychology</i> ,	Retrospective	2	Older (>60years) participants with similar social backgrounds; United Kingdom	No significant differences on socio-demographic characteristics and other background measures	99	NA	NA	Self-reported language questionnaire; English monolingual	Tested background measures, language ability and executive function (mental generativity and speed, working memory, set-shifting and switching, inhibition and management of response)	Not stated	No significant difference on performance of executive tasks

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Ljungberg, J., K., Hansson, P., Adolfsson, R., & Nilsson, L. G. (2016). The effect of language skills on dementia in a Swedish longitudinal cohort. <i>Linguistic Approaches to Bilingualism</i> , 6(1-2), 190-204. doi:10.1075/lab. 14031.lju	Prospective	5	Random sampling from population registry of Umeå; Sweden	Group without dementia: monolinguals were older, less education, lower MMSE scores and less carriers of APOE allele; Group with dementia: monolinguals had less education	835	10	98	Self-reported questionnaire, score of 4 and higher on Likert scale; monolingual	Repeated examination of cognition, functional abilities, and neurological diseases	Age at inclusion, sex, APOE allele	No decreased risk of developing dementia for bilinguals (p=0.50)
Mukadam, N., Jichi, F., Green, D., & Livingston, G. (2018). The relationship of bilingualism to cognitive decline: The	Prospective	6	Longitudinal study participants aged 65 or more	Bilingual participants were younger, more likely to be married, community members,	208	20	0.5	Self-defined, participants speaking another language at home other than English; nonbilingual	Evaluation of language and executive functioning (verbal fluency, description of	Other language, tertiary education, National Adult Reading Test score Wave 1,	Cognitive decline did not differ between bilingual and nonbilingual groups (p= 0.31);

Australian Longitudinal Study of Ageing. <i>Int J Geriatr Psychiatry</i> , 33(2), E249-E256. doi:10.1002/gps.4778				less educated, less likely to have worked previously and more likely to be immigrants				similarities, and Boston naming test)	diabetes, contact with children, "Were you born in Australia?" , smoker, previously working, age left school	bilinguals had lower executive function scores (p=0.051)	
Padilla, C., Mendez, M. F., Jimenez, E. E., & Teng, E. (2016). Bilingualism in older Mexican-American immigrants is associated with higher scores on cognitive screening. <i>BMC Geriatr</i> , 16. doi:10.1186/s12877-016-0368-1	Prospective	5	Participants from SALSA database ≥65 years of age born in Mexico; United States	Bilingual group had more men, higher household incomes, more years of education, and higher rates of stroke	628	Average 5.7	60	Self-reported bilingualism, if spoke English in addition to Spanish; Spanish-speaking monolingual	Comparing cognitive performance on Modified Mini-Mental State Examination (3MS)	Age, gender, education, income, Center for Epidemiologic Studies Depression Scale scores	Better performance by bilingual participant on 3MS (p>0.001*)

Note. Quality assessment score from Newcastle-Ottawa scale (Wells et al., 2013). Point values explained in methods.

\*p = bilinguals significant for cognitive reserve

The purpose of Alladi et al. (2017) was to investigate the role of bilingualism on the onset of different varieties of frontotemporal dementia. Frontotemporal dementia is a type of dementia that is characterized with greater frontal-executive dysfunction. The different types of frontotemporal dementia examined were behavioral frontotemporal dementia, progressive aphasias, and movement disorders such as corticobasal degeneration, progressive supranuclear palsy and motor neuron disease. The hypothesis was that there would be the greatest benefit of bilingualism for the behavioral variant and the smallest benefit for the aphasic forms of frontotemporal dementia.

Results from this study found that only the behavioral variant of frontotemporal dementia was significant for a bilingual effect in the delay of dementia. Progressive nonfluent aphasia, semantic dementia and corticobasal syndrome had close to no effect ranging from 0.4-0.7 years in delay. Progressive supranuclear palsy and frontotemporal dementia-motor neuron disease were insignificant but delayed dementia 4.3 years and 3 years respectively. The bilingual effect for the bilingual behavioral group was independent of confounders such as immigration, education, gender, occupation, and urban vs. rural dwelling. The study was limited by the retrospective study design, the recruitment of the population from a clinical setting, and the subjective and dichotomous definition of bilingualism. Overall, the study concluded that bilingualism serves a protective role against dementia and is domain specific to behavioral frontotemporal dementia. This occurs concurrently through improved executive functions and disadvantaged language functions.

The purpose of Antón et al. (2016) was to investigate the effect of lifelong bilingualism in executive control and the effect of second language proficiency among seniors experiencing cognitive decline. The hypothesis for the first set of experiments was that a bilingual advantage would allow bilinguals to demonstrate better inhibitory control and enhanced monitoring abilities

on verbal and numerical Stroop tests. The hypothesis for the second experiment was that a higher proficiency for a second language would modulate inhibition and monitoring abilities.

Results from this study indicated no such evidence for a bilingual advantage in executive control to delay cognitive decline. Results from the first set of experiments showed no difference between monolinguals and bilinguals in inhibitory and monitoring abilities. In the second set of experiments, degree of bilingualism did not show evidence that language proficiency could modulate inhibitory and monitoring control. There was no immigrant status for any of the participants and all subjects had similar demographic and language backgrounds (only for the first set of experiments). This study found no bilingual advantage for young adults or the elderly. Instead, any potential benefits found for a bilingual advantage is most likely due to other factors outside of bilingualism. The study was limited by cultural differences between the Basque-Spanish bilinguals and Spanish monolinguals.

The purpose of Clare et al. (2016) was to examine executive control amongst the socially and culturally homogeneous population in North Wales, United Kingdom with a range of tests and to better examine how degree of bilingualism impacts cognitive reserve. Language ability was assessed with the Boston Naming Test in English and Welsh, Spot-the-Word Test, the British Picture Vocabulary Scale, and the Welsh Vocabulary Test for Adults. Executive function was assessed across four domains such as mental generativity and speed, working memory, set-shifting and switching, and inhibition and management of response conflict. The variables controlled for were age, gender, educational level, socio-economic status, health status, functional ability, and mood.

Results from this study showed few significant differences between monolingual English and bilingual Welsh/English participants for a range of executive function tasks. In fact, monolinguals performed better on executive function tasks in the domains for working memory and set-shifting and switching. Flaws in the study design were investigated; however, the study

was careful to control for potential confounds, included converging evidence from subjects across the lifespan, measured variables from prior studies that did find a bilingual advantage, included comparisons using cognitive reserve as a proxy, provided a comprehensive set of executive function tests, and recruited a sample size similar to studies in the past. Additionally, there were no significant differences among the groups for socioeconomic status and other demographic variables or cognitive and linguistic abilities. Groups had similar cognitive lifestyle scores and, thus, comparable complex mental activity. Immigration status was not a concern, as the population was a non-immigrant sample from the United Kingdom. Overall, there were few clear differences between monolinguals and bilinguals, with monolinguals performing better in some domains.

The purpose of Ljungberg et al. (2016) was to determine if bilingualism could reduce the risk of dementia among older adults, sixty years of age and older. A prior study, the Betula study, had already found an advantage among bilingual participants in their memory performance. This study would be a ten-year follow-up of the participants from the earlier study to see if the bilingual advantage would continue and postpone the age of onset of dementia. The subject pool consisted of all native-born Swedes that had learned their second language through a formal education. The tools of measurement in this study included a language history questionnaire and a diagnosis of dementia. Potential confounding variables such as age at inclusion, sex and APOE genotype were accounted for.

Results from this study found that there was no significant delay in dementia for bilingual older adults. The authors of this study proposed that there still may be a cognitive benefit of bilingualism due to the previous Betula study on the positive effects of bilingualism on episodic memory. The participants for the current study had retired and consequentially were using their second language less frequently. The study was limited by several factors. First, the time interval for using a second language was relatively large at 0-2 hours per day. Second, a better definition

of bilingualism that was multidimensional and considered language usage and proficiency would strengthen the results of this study. Third, the bilingual subjects from this study acquired their second relatively late in age at nine years of age compared to early childhood, before the age of five, where there is evidence for increased brain development. Additionally, the ten subjects who developed dementia were a relatively small sample; however, this accounted for 10% of the study population which is comparable to the true population. Lastly, none of the participants had immigrant status which can be viewed as a limitation and strength. Overall, it was concluded that the result for bilingualism delaying bilingualism may depend on the frequency of usage of the second language after retirement.

The purpose of Mukadam et al. (2018) was to clarify the link between cognitive decline and bilingualism while factoring for other causes of cognitive decline such as age, sex, education, immigrant status, vascular pathology, history of depression, and social activities. Prior retrospective studies had found a link, while prospective studies found no such benefit to bilingualism to delay cognitive decline. This study was prospective, consisted of a homogenous cohort of literate, non-native English speakers who use their native language at home, and considered the varied factors mentioned earlier. The hypothesis was that bilingual participants would experience slower cognitive decline after adjusting for confounds and that bilinguals would perform better on executive function tests.

Results from this study found that bilingualism did not prevent cognitive decline, and that education level proved to be a better predictor for cognitive decline. The National Adult Reading Test was a strong predictor of years of education and quality of education, and bilinguals had a significantly lower score. The Mini-Mental State Examination was lower for bilinguals, and the rate of decline over time was not different among bilingual and monolingual groups. Many of the bilinguals that had lower scores on the Mini-Mental State Examination were lost over-time due to follow-up. The study was limited by the significant loss of individuals with lower Mini-Mental

State Examination scores, a potential decline in native language proficiency among bilinguals over time, a slight loss of participant recruitment for non-English speakers outside of the home and a lack of dementia diagnosis data. Also, it is important to note that individuals that are not as fluent in English, or do not have as much educational attainment may do worse on the Mini-Mental State Examination since it is a language-based examination. Overall, bilingualism as a sole factor was not found to provide neuroprotective effects; instead educational attainment was a stronger predictor of Mini-Mental State Examination scores in this cohort.

The purpose of Padilla et al. (2016) was to determine the role of bilingualism to modulate cognitive function within the homogeneous Sacramento Latino Study on Aging. Monolingual and bilingual participants consisted of first-generation Mexican American immigrants. Studies in the past have produced inconsistent results from confounding environmental variables and methodological concerns. Immigration, education, socioeconomic and cultural factors are among some of the confounding variables that have limited the strength of studies in the past. Also, differences in cognitive assessments and statistical analyses accounted for some of the methodological concerns of prior studies. Lastly, validity of language of testing and degree of bilingualism was assessed and included a general cognitive screening and more specific assessment of verbal memory.

Results from this study indicated that bilingual participants exhibited better performance than their monolingual counterparts on cognitive screening with the Modified Mini-Mental State Examination, driven by language, executive function, and praxis abilities. A different assessment for verbal memory was not significantly different between bilingual and monolingual participants. The two factors, language of testing and the degree of bilingualism, did not have significant impact on results. After a six-year follow-up period, bilingual and monolingual groups showed similar rates of decline on the Modified Mini-Mental State Examination and verbal memory assessments. The study was limited by differences in regional patterns of immigration

from Western and Northern Mexico, and possibly subtle cultural differences. Also, they were unable to account for age of immigration and age of acquisition for the English language. Lastly, there were differences in demographic variables such as the bilingual group was more male, more educated, had a higher monthly household income, and higher prevalence of stroke.

Monolinguals had more clinical depression. Data on pre-morbid IQ or length of residence in the United States which Padilla and colleagues suggested may have allowed for more robust statistical analysis.

## CHAPTER FIVE

### Conclusion

This systemic review brought together and appraised the most recent published evidence of Alzheimer's disease and dementia among multilingual, bilingual and monolingual individuals to observe the possibility of an advantage of speaking more than one language in regard to dementia-related diseases. A systematic review by Mukadam et al. (2017) found no significant differences in level of cognitive impairment among prospective studies that investigated differences between monolinguals and bilinguals, while retrospective studies found on average a 4.5-year delay in cognitive decline for bilingual groups. Prospective studies are usually more reliable than retrospective studies since prospective studies have less recall bias and can more accurately control for confounders. Mukadam et al. (2017) determined that bilingualism does not provide any cognitive benefit.

This systematic review replicates and updates the findings of Mukadam and colleagues. The studies assessed for this project included retrospective and prospective studies that focused on cognitive reserve and neural reserve. Unlike Mukadam and colleagues, statistical analysis was unable to be completed due to the methodological differences between cognitive reserve and neural reserve studies. It should also be noted that a large majority of the studies were performed abroad, and this might have implications on the results of such studies.

Of the studies specific to solely cognitive reserve, two, Alladi et al. (2017) and Padilla et al. (2016), reported a cognitive advantage for bilinguals in comparison to monolinguals, whereas five studies reported no difference among the two language groups in cognition. One of the two studies reporting a significant difference for bilinguals found a six-year delay of behavioral frontotemporal dementia onset (Alladi et al., 2017). While this is an interesting finding, it should not go without notice that behavioral frontotemporal dementia is a specific variant of dementia

and does not apply to all dementia-related diseases. Other frontotemporal dementia syndromes did not appear to be significantly delayed due to the presence of bilingual language skill. Thus, this finding only contributes to a specific variant of dementia and not to Alzheimer's disease. Additionally, this study was retrospective, clinically based, and defined bilingualism subjectively rather than objectively which is a more reliable method of measurement (Mukadam et al., 2017).

Padilla et al. (2016) reported better cognitive performance on the Modified Mini-Mental State Examination and concluded that bilinguals could withstand greater cognitive deterioration before reaching a clinical diagnosis of mild cognitive impairment or dementia. No dementia-related disease diagnoses were made in the study design, so this was a prediction only. Bilingual participants were, again, more educated and had higher incomes. Bilingualism was subjective, and there was no degree of bilingualism included in the study design.

Four of the seven studies on cognitive reserve reported no significant difference in cognitive performance for bilingual participants. One study focused particularly on executive function through performance on monitoring or inhibitory control (Anton et al., 2016). Furthermore, they stated that there was no evidence of a bilingual advantage and, thus, no evidence that bilingualism delays dementia-related diseases. The participant pool was small, and the Basque-Spanish bilingual group could be considered a cultural minority and different from the Spanish monolingual group. Additionally, the study was retrospective, and bilingualism was self-reported and subjective.

The study by Clare et al. (2016) also found no difference on executive function between bilinguals and monolinguals. In fact, monolinguals performed better than bilinguals on some measures of executive function. However, this study concluded that it would be unlikely for there to be cognitive reserve to delay cognitive decline and the study reported on behavioral and not brain functional differences. The study was retrospective, and bilingualism was subjective. However, the participants did not differ significantly on socio-economic activity, cognitive ability

or language abilities which are measures that add uncertainty to results. The sample size was small; however, the article argued that similar sample sizes yielded significant differences for a bilingual advantage in the past.

The study by Ljungberg et al. (2016) directly reported on dementia and found no decreased risk in developing dementia between monolinguals and bilinguals. Dementia was classified as a diagnosis of Alzheimer's disease, vascular dementia, Lewy body dementia, frontal lobe dementia, Parkinson dementia and unspecified dementia. The study was done prospectively with a large, randomly sampled population. One flaw in the study was that bilingualism was defined subjectively and bilingual participants reported relatively late ages of acquisition for second languages. Additionally, the bilingual group stopped using their second language as frequently after retirement which could have impacted the results. However, the study scored moderately well on the quality assessment.

The last study to have reported no significant differences in regard to cognitive reserve was the study by Mukadam et al. (2018) which reported no difference in cognitive decline. Bilinguals in this study had lower executive function skills. The study had significant loss of subjects to follow-up, and many of the subjects lost were those that scored lower on the Mini-Mental State Examination. Additionally, the Mini-Mental State Examination is biased towards those that are more fluent in English and more educated. The National Adult Reading Test added strength to this bias but does not remove it. Also, there was no data collected for dementia diagnosis and bilingualism was subjective.

In conclusion based on the results from the studies on cognitive reserve and the validity of their results, there is not strong evidence for bilingualism and multilingualism to provide just cognitive reserve to delay Alzheimer's disease. The studies that did report significant differences between bilinguals and monolinguals were either interested in specific types of dementia related disease or were unable to gather a diagnosis for dementia. These studies were specific to certain

populations that were culturally different, more educated, had higher incomes, etc. Some of the studies with no significant differences also faced challenges with education and socioeconomic status; however, they were controlled for, and the studies appeared more reliable. Cognitive reserve and behavioral performance alone do not provide strong evidence to delay Alzheimer's disease.

While cognitive reserve alone does not overwhelmingly suggest evidence to delay dementia, some of the studies that focused on neural reserve and cognitive reserve found that bilingualism and multilingualism could provide a benefit to prevent against cognitive decline. Methods ranged from glucose uptake to measure brain metabolism or activity, brain scans to measure differences in brain matter and gray matter volume and thus the number of neural networks, and behavioral assessments for cognitive reserve and executive function. All of the studies were done retrospectively with none of the sample sizes exceeding one-hundred participants.

Four studies reported on increased gray matter volume in specific areas for bilingual participants. Anderson et al. (2018) identified the left superior longitudinal fasciculus as a key region for neural reserve in bilinguals. This region connects integral areas of the language network within the brain such as Broca's area and receptive language areas in the temporal lobes. Borsa et al. (2018) found that structures within the right hemisphere were better preserved than structures in the left hemisphere for bilingual participants. Additionally, gray matter volume of the anterior cingulate cortex was a strong predictor of cognitive control for bilinguals. Del Maschio et al. (2018) identified the bilateral anterior cingulate cortex, prefrontal cortex, and inferior parietal lobule as areas of increased gray matter volume among bilinguals while experiencing overall widespread brain deterioration. These areas were identified as key regions of the executive control network. The groups differed in cultural backgrounds. Duncan et al. (2018) identified several key brain regions significant for neural reserve: the right and left inferior frontal

gyri, left medial superior frontal gyrus, right ventromedial prefrontal cortex, left and right anterior temporal gyri, left parietal lobule, left and right cerebellum, and right cerebellar tonsil which exhibited greater gray matter volume in mild cognitively impaired and Alzheimer's disease patients. Additionally, multilinguals exhibited greater deterioration of the posterior parahippocampal gyri and rhinal sulci, but greater gray matter volume in language control brain regions and better episodic memory performance to compensate. The participant pool was restricted to clinic-based participants. Three specific areas that were mentioned across multiple studies were the anterior cingulate cortex, prefrontal cortex, and parietal lobule. Additionally, all of the studies reported that brain differences and usage of a second language provide neural reserve.

Estanga et al. (2017) found a lower prevalence of preclinical Alzheimer's disease among early bilinguals, or those who acquired a second language at an early age, and a decrease in cerebrospinal fluid total-tau protein, a known sign associated with Alzheimer's disease. Additionally, the findings supported the cognitive reserve theory in that bilingualism moderated Alzheimer's disease bio-markers and decreased executive function. The quality appraisal of Estanga et al. found that the participant pool was smaller than other prospective studies included in this review and a limited number of participants did not contribute a cerebrospinal fluid sample for analysis. The study also defined bilingualism subjectively.

Kowoll et al. (2016) and Perani et al. (2017) both reported more glucose reuptake and metabolism for bilingual participants. This method allowed the studies to measure neuronal activity and viability. Perani et al. (2017) identified that glucose metabolism was increased in the frontoparietal executive control network and default mode network. Bilingual participants also demonstrated severe left hemisphere hypometabolism (less metabolically active). Despite such brain differences, bilingual participants outperformed monolingual participants on short-term and long-term verbal memory and visuospatial tasks, and not on tasks associated to language. Kowoll

et al. (2016) identified that the right gyrus frontalis inferior, left cerebellum, right gyrus temporalis medius and left inferior parietal lobe were less metabolically active for bilingual mild cognitively impaired and Alzheimer's disease patients without differing from the cognitive impairment of monolingual patients. Both studies affirmed the neural reserve theory that structural brain deterioration could be overcome through compensatory networks to provide cognitive resilience.

Across the studies for neural reserve and cognitive reserve, there were a variety of communalities and observations that stood out. Within the studies just looking into cognitive reserve, the only studies that had significant results for an advantage of bilingualism and multilingualism against dementia either found significant results for a specific and less common type of dementia such as behavioral frontotemporal dementia (Alladi et al., 2017) or had no diagnosis of dementia (Padilla et al., 2016). Additionally, the studies for cognitive reserve dealt with limitations such as cultural differences, education level, socioeconomic status, retirement age, degree of bilingualism and age of acquisition. Within the studies for neural reserve and cognitive reserve, all of the studies reported evidence for neural reserve. Neural and cognitive reserve was limited to a select three studies (Duncan et al., 2018; Estanga et al., 2017; Perani et al., 2017). In the interest of structural brain differences, the areas of the anterior cingulate cortex, prefrontal cortex and parietal lobe were a communality across the studies. However, all of the studies on neural reserve were retrospective, had smaller sample sizes, and clinically based populations.

This paper examined the evidence of structural and behavioral brain differences in providing neural and cognitive reserve to bilinguals and multilinguals as a protection against Alzheimer's disease and other forms of dementia. While these are two separate measures with different implications, they aim to answer the same question, that is, is there a benefit of learning and using more than one language to prevent against cognitive decline in Alzheimer's disease and

other dementia-related diseases? By separating the studies into cognitive reserve and both neural and cognitive reserve, several observations could be drawn from the results. There does not appear to be overwhelming evidence for bilingualism and multilingualism to provide cognitive reserve and delay dementia; however, when combined with methodologies for neural reserve there seems to be more interesting results with this broader approach. The more structural approaches to the question with neural reserve methods were usually balanced with behavioral, cognitive reserve methods. This interdisciplinary approach between behavioral disciplines and anatomical and physiological disciplines could provide more encompassing and intriguing results. This brought to mind recommendations about the approach to this topic. This topic would benefit from studies including both neural and cognitive reserve, prospective study designs, objective definitions of bilingualism with age of acquisition and proficiency, adjustment of confounders (age, sex, education, immigration status, socioeconomic status, vascular disease, etc.), randomization of the population sample (not clinically based), and a clinical and reliable diagnosis.

This project was limited in that there was no meta-analysis done on the collected data from the included studies. This possibility was considered; however, the dataset was too heterogeneous to provide strong and meaningful statistical meta-analyses.

There appears to be no significant evidence that bilingualism and multilingualism provides cognitive reserve in delaying dementia-related diseases and cognitive decline. However, it appears that there is a structural benefit through neural reserve for bilingualism and multilingualism in increasing compensatory neural networks. These compensatory networks may allow bilinguals and multilinguals to withstand severe brain structure deterioration without showing behavioral symptoms. This may have implications on age of diagnosis or diagnostic practices. Thus, bilingual and multilingual Alzheimer's disease or mild cognitively impaired patients could experience significant brain deterioration in comparison to their monolingual

counterparts while behaving similarly, or better on language and cognitive abilities. To sum up, it is hard to draw a firm conclusion on the role of bilingualism and multilingualism to delay Alzheimer's disease and other forms of dementia with such varying results and method practices. Future studies should encompass both neural and cognitive reserve methods through controlled long-term studies factoring for a well-defined and accurate measure of language use and acquisition, confounders, a sample representative of the entire population, and a clinical and reliable diagnosis. There is still more high-quality research needed for this topic.

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