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REVIEW OPEN ACCESS

The Effects of Bilingualism and Multilingualism on Alzheimer's Disease Progression: A Systematic Review

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Abstract

Introduction: Neurodegenerative disorders, including Alzheimer's disease (AD) can result in memory dysfunction and cognitive impairments. Bilingualism and multilingualism have been shown to have preventative effects on AD due to influence on brain regions and the improvement of cognitive reserve (CR). The paper analyses studies explicating the role of bilingualism and multilingualism in AD progression by evaluating their effects on CR, brain pathology, and behavioral function. We hypothesize that both bilingualism and multilingualism delay onset of AD and help prevent symptoms related to AD by improving cognitive functioning.

Methods: For this comprehensive comparative analysis, we reviewed empirical research articles found through PubMed and other databases to investigate the effects of bilingualism and multilingualism on AD manifestation. Keywords such as ageing, multilingualism, bilingualism and AD were used, and research published before 2000 was excluded. Specific focus was placed on AD onset time and symptoms as a framework for severity evaluation. A total of 13 studies were chosen to be included in this review.

Results: Results suggest bilingualism and multilingualism play a role in the strengthening of different preventative factors, such as CR. Improved effects are evident throughout various brain structures, such as improved resistance to grey matter deterioration in bilinguals and multilinguals with AD. These protective effects are also observed in behavioural functionality, with improved executive function present in bilinguals and multilinguals. The effects of multilingualism on AD seem to be stronger than those of bilingualism.

Discussion: Bilinguals and multilinguals have a stronger CR, which is linked to improved neuroplasticity and neural circuit efficiency; these contribute to ameliorated memory retention. By analyzing the effect of bilingualism and multilingualism on AD progression, we aim to improve the understanding of therapeutic targets to alleviate the impact of symptoms and provide further avenues for testing.

Conclusion: Our review will aid in establishing alternative means of treatment and preventative methods to decrease cognitive impairment in AD patients. Elucidating bilingualism and multilingualism mechanisms of action in AD progression will strengthen our understanding of its protective measures. This analysis will allow exploration into new avenues with the ultimate goal of reducing the incidence and impact of AD.

Keywords: bilingualism; multilingualism; Alzheimer's disease; neurodegeneration; cognitive reserve; dementia; protective effects; brain deterioration

Introduction

Alzheimer's disease (AD) is a neurodegenerative disease (ND) that is one of the most common forms of dementia; it impairs crucial cognitive functions such as the storage and retrieval of memory [1]. AD affects 58 million people worldwide, with 9.9 million new cases every year [2]. Risk factors associated with AD include increasing age, genetics, and linked vascular diseases [3]. Although the specific cause of AD has not been defined as of yet, it has been correlated with amyloid plaques and tau deposits in the brain. The plaques and deposits interfere with communication between brain regions and neural functioning, thus impairing cognitive functions [4]. As a result of having a climbing aging population, AD's high prevalence continues to rise. Understanding the preventative factors of the disease could subsequently

decrease its incidence in the population. One such factor is cognitive reserve (CR), which has been inferred to be lower in those with AD than their healthy counterparts.

Cognitive reserve refers to the difference between brain pathology and function. One can increase CR by exercising regularly, sleeping, and eating healthy. Given a group of people with the same degree of neurodegeneration, their abilities to perform a task can still vary based on their CR, with those having a higher CR outperforming those with a lower CR [5]. Consequently, a high CR would act to prevent the functional symptoms associated with an ND such as AD, regardless of an individual's neurological pathology.

Recently, bilingualism and multilingualism have been shown to increase CR; subsequently, speaking more than one language has been hypothesized to delay AD onset [6]. According to a 2021 study, there are currently over 33 million bilingual individuals globally, with the majority of those being between the ages of 16 to 24 [7]. Of these 33 million people, around 5 million are categorized as multilingual, meaning they speak more than two languages fluently [7].

Studies conducted have found that by engaging in language learning, such as developing bilingualism or multilingualism, individuals can strengthen neural efficiency thereby decreasing the risk of AD as well as reducing the symptoms associated with the disease [8]. The effects that bilingualism and multilingualism have on brain structure and function have become the focus of numerous investigations, resulting in implications on the studies being conducted and therapeutic approaches being explored for ND. Recent studies have shown that multilingual and bilingual individuals have different volumes of cortical and subcortical grey matter, as well as white matter tracts connecting these two regions, dependent on usage of multiple languages [9]**.** Unsurprisingly, these brain areas correlate to language learning, semantics, and speech production [10]. Moreover, these alterations are a result of neuroplasticity, which is also seen to aid individuals while learning and utilizing a new skill [11]. Additionally, the use of more than one language has been thought to increase CR. Alternating between languages requires complex cognitive processes and attention [12], which may exercise the brain's neuroplasticity, thus delaying the neurodegeneration that plays a role in AD. This hypothesis was further supported by some studies indicating that bilingual individuals experienced delayed dementia symptoms [12, 13].

However, presently, the results of existing literature regarding the exploration of how bilingualism and multilingualism affect CR, as well as the structural and functional changes occurring in the brain due to these effects, specifically in the context of AD, have not been cumulatively analyzed and explored while including recent studies. In an effort to supplement present literature, the studies examined in this review include those exploring said effects. As such, the focus of this review will be to examine the extent to which bilingualism and multilingualism influence different AD-contributing factors, compared to monolingualism, along with how the two compare with each other. In doing so, this examination will explore the potential for language-related therapeutic avenues for individuals with AD, as well as shed light on the association between the number of languages spoken and AD symptom risk/onset.

Methods

A systematic literature review was conducted to analyze the effects of bilingualism and multilingualism on AD. As shown in Figure 1, the PubMed, Google Scholar, ScienceDirect and Ovid databases were used to perform a search of relevant literature, followed by a thorough review of shortlisted articles. The search terms included the primary keywords "bilingualism" OR "multilingualism" AND "Alzheimer's disease" OR "AD", with the secondary keywords "neurodegenerative diseases", "cognitive reserve", "diagnosis", "longitudinal study", and other related keywords. As a part of the inclusion criteria, only empirical studies were considered to be reviewed. Further inclusion criteria for studies included those written in English, peer-reviewed, and published after the year 2000. Exclusion criteria also included any meta-analyses, literature review articles, dissertations, editorials, and commentaries. A total of 32 articles were retrieved for full-text review. All studies retrieved were examined to ensure that they explicitly included accurate assessments of the participants 'diagnoses of AD following credible diagnostic criteria. Out of the articles reviewed, 13 were selected to be included in this review.

Results

Current literature establishes a substantial role of bilingualism and multilingualism in AD. In this review, we discuss data indicating the role of the cognitive reserve in this relationship, as well as structural and functional changes resulting from bilingualism and multilingualism.

Bilingualism

Cognitive Reserve

Presently, evidence indicates a substantial impact of bilingualism on the onset of AD, delaying the age at which the disease is developed [14-16]. A case study conducted with individuals with AD dementia found a statistically significant difference in onset time, after accounting for confounding variables such as education level [14]. Other epidemiological data has also shown a later onset of AD in individuals who are bilingual when compared to monolingual individuals, indicating possible contribution of bilingualism to cognitive reserve [17]. Studies have also examined the relationship between bilingualism and mild cognitive impairment (MCI), a prodromal stage of AD onset [15]. Executive function tests conducted with bilingual and monolingual individuals show that the onset of AD symptoms is delayed by 7.3 years in bilingual individuals compared to monolingual individuals [15].

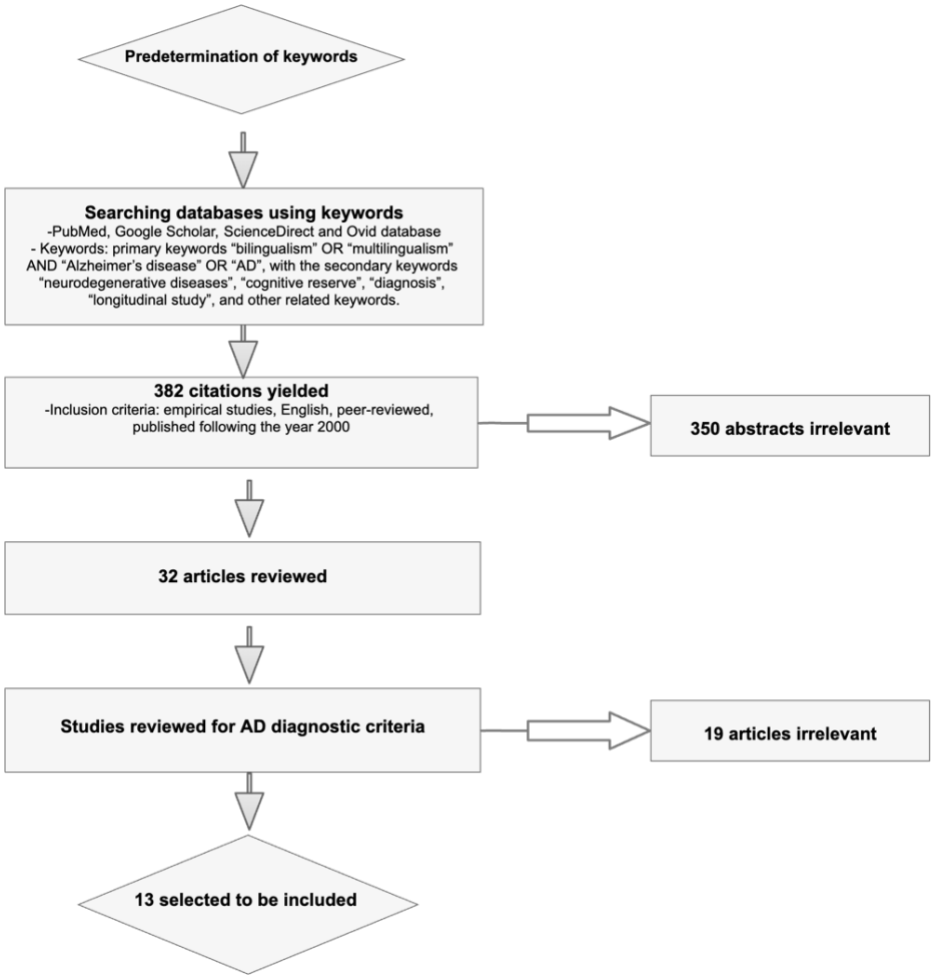

Figure 1. Flowchart of the methodology of the literature review (created with Creately.com)

Brain Structure

Additional studies have examined the role of bilingualism in neural structural changes in those with AD. The impact of bilingualism on neuroanatomy is well studied; bilinguals tend to have a more efficient neural network as well as greater structural connections than monolinguals [18]. Compared to monolinguals, bilinguals have greater bilateral expansion of the putamen and thalamus, as well as expansion of the left globus pallidus and right caudate nucleus [19]. This suggests that bilinguals develop a more complex phonological system compared to monolinguals, leading to potentially stronger subcortical network development and neural connections [19]. Studies including individuals with AD have also been conducted: computerized tomography (CT) scans performed on bilingual and monolingual individuals with AD showed greater brain atrophy in bilingual individuals than monolingual individuals at time of disease onset, indicating the need for more substantial damage in a bilingual individual's brain before symptom onset [20].

Cognitive & Functional Changes

Previous studies have also illustrated the role of bilingualism in functional changes in AD individuals. For example, one study used functional magnetic resonance imaging (fMRI) to examine brain metabolism and neural connectivity during a perceptual task in older bilingual and monolingual individuals [21]. The purpose was to analyze the structural and metabolic differences in the brain between bilinguals and monolinguals. It was found that bilingual individuals performed better than monolinguals on the task switching experiment ($p<0.007$); this was accompanied by recruiting lower frontal brain activation, indicating a lesser age-related decline in bilinguals than monolinguals [21]. Specifically, in AD, positron emission tomography (PET) scans in bilingual individuals illustrated increased cerebral hypometabolism compared to monolingual individuals, along with greater neural connectivity in executive control and the default mode networks in bilingual individuals [16]. Consequently, bilinguals had a beneficial increase in metabolism in the left

hemispheric areas and inferior frontal gyrus of the brain, which may have compensated for the neurodegeneration caused by AD. This finding was further supported by another study, which also demonstrated greater cerebral hypometabolism in bilingual AD individuals [22].

Multilingualism

Cognitive Reserve

Studies have been conducted specifically examining the long-term effects of learning more than two languages as well. For the purposes of the present review, multilingualism is defined as proficiency in three or more languages. A worldwide analysis that was conducted in 2016 has shown that multilingualism has protective effects for AD, delaying the onset of the disease and specifically contributing to the cognitive reserve [23]. This study included bilinguals as well, comparing the results solely to monolinguals. Another study conducted comparing bilinguals and multilinguals has shown a significant protective effect for all multilingual participants, including both immigrants and nonimmigrants [13]. The results were more significant ($p<0.001$) for the multilingual participants when compared to bilingual participants.

Structural Aspects

Structural studies conducted with multilingual individuals with AD have shown promising results regarding the protective effects of multilingualism. One such study examined cortical thickness to determine grey matter deterioration in multilingual individuals with AD as compared to monolingual individuals with AD [24]. They found greater cortical thickness in multilinguals and lesser grey matter atrophy, indicating a possible role of multilingualism in grey matter thickness.

Functional & Behavioural Changes

Further cognitive and functional changes have also been seen in studies conducted on multilingual AD individuals. One specific study conducted on trilinguals measured the onset of AD as well as response times on behavioural Simon and flanker tasks and memory generalization tasks [25]. Compared to bilinguals, trilinguals seemed to have a better performance in some aspects of the experiment conducted, such as CR measured by the age of AD onset, and weaker performance for memory generalization ($p<0.001$). This paper also provides more evidence concerning the role of language in neuroplasticity. Unlike previous studies, Schroeder et al. (2017) discusses the possibility that trilinguals may have improved cognitive functionality than bilinguals due to the higher cognitive demands of using more than two languages.

Table 1. Results Summary Table (Created Using Microsoft Excel)

Bilingualism/ Multilingualism	Effects	Citation Number	Year Published	Authors	Protection against AD	p-value	Number of Participants
Bilingualism							
	Cognitive Reserve						
		[14]	2013	Alladi et al.	There is a statistically significant difference in AD onset time for bilingual individuals compared to monolingual individuals.	p=0.013	n=240
		[17]	2010	Craik, Bialystok & Freedman	Compared to monolinguals, bilingual individuals experience a delayed onset of AD by 5.1 years. This indicates a potential contribution of bilingualism to cognitive reserve.	p<0.0001	n=211
		[15]	2014	Bialystok et al.	Executive function tests revealed that bilingual individuals have a delayed onset of AD by 7.3 years compared to monolinguals.	p<0.0001	n=75
	Brain Structure						
		[18]	2014	García-Pentón et al.	Bilinguals have more connected sub-networks than monolinguals. These highly connected sub-networks are involved in language processing.	p<0.01	n=26
		[19]	2009	Bialystok et al.	Bilinguals have a greater expansion of the bilateral putamen and thalamus, left globus pallidus, and right caudate nucleus, compared to monolinguals	No Indicated p-values	No Indicated Number of Participants
		[20]	2012	Schweizer et al.	Bilinguals have higher values in the temporal horn ratio and third ventrical ratio measures, which indicates more atrophy.	p=.02; p=.002	n=40
	Cognitive & Functional Changes						
		[21]	2013	Gold et al.	Bilingual individuals performed better than monolingual individuals on the task switching experiment, indicating lesser age related decline	p<0.007	n=80
		[16]	2017	Perani et al.	Bilinguals had a higher CR, and there is metabolic evidence that these bilignauls have neuroprotection against AD. There was also a positive correlation between the usage frequency of the second language and the neuroproctective effect.	p<0.005	n = 40
		[22]	2021	Sala et al.			
Multilingualism							
	Cognitive Reserve						
		[23]	2016	Klein et al.	Multilinguals tend to have neuroprotection against cognitive decline. The paper highlights gaps in literature as there is not much research into this topic.	p<0.05	n = 73
		[13]	2010	Chertkow et al.	Multilinguals have significant neuroprotection against AD., however found no significant evidence of this neuroprotection in bilinguals in terms of age diagnosis. Both multilinguals and bilinguals had delayed diagnosis time compared to monolinguals.	p<0.001	n=184
	Structural Aspects						
		[24]	2018	Duncan et al.	Multilinguals have greater cortical thickness and lesser grey matter atrophy than monolinguals, which would imporve episodic memory.	p = 0.001	n = 94
	Functional & Behavioural Changes						
		[25]	2016	Schroeder et al.	Trilingual individuals have a larger cognitive researve than biling	p < 0.001	n = 203

Discussion

This systematic review aims to elucidate the relationship between bilingualism or multilingualism and CR, as well as the onset and symptom risk of AD. Prior to this, there has been a lack of reviews examining this concurrent relationship in detail. Predominantly, studies examined in this review indicate that bilingualism induces protective mechanisms against AD as compared to monolingualism, through its contribution to CR. The findings indicate that bilingualism plays a strong contributing role in maintaining the cognitive reserve. Specifically, the onset of AD symptoms is delayed significantly in bilinguals as compared to monolinguals. This finding is supported by studies conducted on structural and functional aspects of the brain, and executive function tests as well [15]. These results strengthen the literature supporting a connection between bilingualism and the cognitive reserve. Furthermore, it was found that bilinguals depend more on the posterior and subcortical regions of the brain, indicating that they are less vulnerable to ageing-related decreased cognition as compared to monolinguals [24]. These results taken together elucidate the role of bilingualism in neuroprotective mechanisms in the context of AD.

The studies conducted on multilingualism have promising results as well; it has been found that multilingualism significantly contributes to CR, thus delaying the onset of symptoms of AD, perhaps even more than bilinguals [14]. These results are further supported by experiments conducted examining the changes in brain structure: decreased structural neurodegeneration, specifically grey matter deterioration, is observed for multilinguals as compared to monolinguals [24]. This could also potentially contribute to alleviating cognitive symptoms due to AD. It also points out the potential implications of multilingualism on protecting the cognitive reserve. Further, behavioural changes point towards enhanced executive functions and memory performance in multilingual individuals with AD as compared to bilinguals, indicating that multilingualism may have additive protective effects than bilingualism. This indicates a role in the cognitive reserve, perhaps more so for multilingual individuals. However, it remains unclear the extent to which multilingualism has protective effects above and beyond bilingualism – an idea that could be explored further in future studies.

CR is a major contributor to delaying AD's onset time and decreasing symptom severity; it could potentially provide a protective effect strengthened by being bilingual or multilingual [14,23]. The studies conducted demonstrate that increasing the number of languages an individual is proficient in could result in a higher 'demand 'for cognitive function [25]; consequently, this would result in better protection from AD by strengthening one's CR, in turn causing the development of stronger neural networks due to increased cognitive demand. Higher cognitive function is linked with higher neuroplasticity, thus improved CR, leading to a higher chance of AD prevention or delay. More efficient neural networks are indicative of a stronger CR, as shown by studies examining structural neuroimaging [20,21,24,25]. Thus, a greater CR is indicative of better executive functions, providing a possible explanation for the delay of AD symptom onset.

Many neural mechanisms of CR remain unknown, yet these play a significant role in improving neural health. One such mechanism includes improved metabolic activity in the entorhinal cortex (EC) circuit due to an enhanced CR [26]. This results in greater efficiency in neural networks (i.e., an increase of oxygen and glucose), benefitting the health and alleviating AD pathology by increasing myelination of axons in the EC circuit [26]. Increasing the myelination of axons decreases the chances of deterioration of the axons and improves synaptic connectivity. Therefore, bilinguals and multilinguals who repeatedly engage the EC circuit over their lifespan may have improved episodic memory and executive function, resultantly delaying AD symptom onset. The improved metabolism in the EC circuit has also been found to increase angiogenesis, thus improving brain functionality. Bilinguals and multilinguals depend more on the EC circuit than monolinguals, indicating improved synaptic function [26]. The relationship between bilingualism/multilingualism and the EC circuit, and its effects, could be examined in further detail for potential clinical interventions.

The studies analyzed provide an optimistic potential for language-related therapies for AD. However, it is important to note that although bilingualism and multilingualism are major lifestyle factors that contribute to decreasing the risk and symptoms of AD, they do not seem to act as a cure or means for reversal. The integration of bilingualism and multilingualism in everyday life has been estimated to delay AD symptoms from between 4.5 to 5 years [14,17]. On the other hand, there has been debate as to whether the findings presented in this paper delays AD, or simply decreases the severity of its symptoms, masking the physical manifestation of AD pathology until later in life.

The studies reviewed are not without limitations; these include variable study group characteristics, data analysis techniques, and time-frame discrepancies. Further, there are diverse methodologies as some studies use a single study approach, whereas others use age-of-onset methods. Both methods are valid, but provide difficulty in creating consistency within this review. There is also no consistent minimum usage of the second or third language. This raises an interesting question to explore further: what is the minimum usage of an additional language to delay the onset of AD? Predictably, the participant's proficiency in each language varied, contributing to a lack of consistency within study groups. Furthermore, the role of confounding variables such as socioeconomic factors, education, and

physical health on AD risk was not accounted for by all of the studies; future research should continue assessing such demographic variables.

As mentioned previously, the role of bilingualism and multilingualism has facilitated a new understanding of how CR can pose a potential therapeutic avenue for AD. Consequently, schools should encourage their students to become proficient in more than one language in hopes of delaying possible cases of AD and other dementias. Older individuals should be encouraged to use multiple languages in their daily lives, whether it is through conversing, entertainment, or learning. Most importantly, future research should be done in analyzing the way in which bilingualism and multilingualism delay AD symptoms.

Conclusion

Ultimately, studies analyzing the effects of bilingualism and multilingualism on CR, cognitive functions, and brain structures provide a baseline for potential future studies. The relationship between the effects of bilingualism's and multilingualism's effects on CR could be tested further to solidify whether multilingualism has greater protective effects than bilingualism. Indeed, it is essential to acknowledge the limitations of the studies examined in this paper, as they lack the accuracy of randomized controlled trials. Further testing into therapeutic avenues exploring bilingualism and multilingualism as a protective mechanism against AD could strengthen previously established foundations of understanding. On the whole, it is apparent that bilingualism and multilingualism play a significant role in improving preventative factors and delaying the onset time as well as reducing the symptom severity of AD.

List of Abbreviations Used

AD: Alzheimer's disease
CR: cognitive reserve
CT: computerised tomography
EC: entorhinal cortex
fMRI: functional magnetic resonance imaging
MCI: mild cognitive impairments
ND: neurodegenerative disorders
PET: positron emission tomography

Conflicts of Interest

The author(s) declare that they have no conflict of interests.

Ethics Approval and/or Participant Consent

Since this is a systematic review, an ethics approval and/or participant consent was not required.

Authors' Contributions

VAM: contributed to the conception and analysis of the review, drafted and revised the content, and gave final approval of the version to be published.
IMB: contributed to the conception and analysis of the review, drafted and revised the content, and gave final approval of the version to be published.
GAM: contributed to the conception and analysis of the review, drafted and revised the content, and gave final approval of the version to be published.

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