Cet article a été accepté pour publication dans American Journal of Speech-Language Pathology (https://doi.org/10.1044/2023_AJSLP-23-00137)

Exploring spoken discourse and its neural correlates in women with Alzheimer's disease with low levels of education and socioeconomic status

Neural correlates in low-SES women with Alzheimer

Bárbara Luzia Covatti Malcorra[1*], Alberto Osa García[2,3*], Karine Marcotte[2,3], Hanna de Paz[2,3], Lucas Porcello Schilling[4,5,6,7], Irênio Gomes da Silva Filho[5], Ricardo Soder[4,6], Alexandre da Rosa Franco[8,9,10], Fernanda Loureiro[5], Lilian Cristine Hübner[1,7,11]

[1] School of Humanities (Linguistics Department), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil

[2] Centre de recherche du Centre intégré universitaire de santé et de services sociaux du Nord-de-l'Île-de-Montréal, Hôpital du Sacré-Cœur de Montréal, Montréal, Québec, Canada

[3] École d'orthophonie et d'audiologie, Faculté de médecine, Université de Montréal, Montréal, Québec, Canada

[4] School of Medicine, Graduate Course in Medicine and Healthy Sciences, Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil

[5] School of Medicine, Graduate Course in Biomedical Gerontology, Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil

[6] Brain Institute of Rio Grande do Sul (InsCer), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil

[7] Institute of Geriatrics and Gerontology (IGG), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil

[8] Center for Biomedical Imaging and Neuromodulation, The Nathan S. Kline for Psychiatric Research, Orangeburg, NY, USA

Cet article a été accepté pour publication dans American Journal of Speech-Language Pathology (https://doi.org/10.1044/2023_AJSLP-23-00137)
[9] Center for the Developing Brain, Child Mind Institute, New York, NY, USA

[10] Department of Psychiatry, NYU Grossman School of Medicine, New York, NY, USA

[11] National Council for Scientific and Technological Development (CNPq), Brasília, DF, Brazil

* Bárbara Luzia Covatti Malcorra and Alberto Osa García share first authorship.

Corresponding author: Bárbara Luzia Covatti Malcorra – 6681 Ipiranga Ave (PUCRS), Building 8, room 403, Partenon, Porto Alegre – RS – Brazil – ZipCode 90670-000. E-mail: barbaraluz.malcorra@gmail.com

Conflict of interest: There is no conflict of interest to declare.

Cet article a été accepté pour publication dans American Journal of Speech-Language Pathology (https://doi.org/10.1044/2023_AJSLP-23-00137)

Abstract

Background: Early impairments in spoken discourse abilities have been identified in Alzheimer's disease (AD). However, the impact of AD on spoken discourse and the associated neuroanatomical correlates have mainly been studied in populations with higher levels of education, although preliminary evidence seems to indicate that socioeconomic status (SES) and level of education have an impact on spoken discourse.

Purpose: To analyze microstructural variables in spoken discourse in people with AD having low-to-middle SES and low level of education, and to study their association with grey matter (GM) density.

Method: Nine women with AD and 10 matched (age, SES, and education) women without brain injury (WWBI) underwent a neuropsychological assessment, which included two spoken discourse tasks, and structural magnetic resonance imaging. Microstructural variables were extracted from the discourse samples using NILC-Metrix software. Brain density, measured by voxel-based morphometry, was compared between groups, and then correlated with the differentiating microstructural variables.

Results: The AD group produced a lower diversity of verbal time moods, fewer words and sentences than WWBI, but a greater diversity of pronouns, prepositions and lexical richness. At the neural level, the AD group presented a lower GM density bilaterally in the hippocampus, the inferior temporal gyrus, and the anterior cingulate gyrus. Number of words and sentences produced were associated with GM density in the left parahippocampal gyrus whereas the diversity of verbal moods was associated with the basal ganglia and the anterior cingulate gyrus bilaterally.

Conclusions: The present findings are mainly consistent with previous studies conducted in groups with higher levels of SES and education, but they suggest that atrophy in the left inferior temporal gyrus could be critical in AD in populations with lower levels of SES and education. This research

Cet article a été accepté pour publication dans American Journal of Speech-Language Pathology (https://doi.org/10.1044/2023_AJSLP-23-00137)
provides evidence on the importance of pursuing further studies including people with various SES and education levels.

What is already known on this subject.

Spoken discourse has been shown to be affected in Alzheimer disease, but most studies have been conducted on individuals with middle to high socioeconomic status and high educational levels.

What this study adds.

The study reports on microstructural measures of spoken discourse in groups of women in the early stage of Alzheimer's disease and healthy women, with low-to-middle socioeconomic status and lower levels of education.

Clinical implications of this study.

This study highlights the importance of taking into consideration the socioeconomic status and education level in spoken discourse analysis and in investigating the neural correlates of Alzheimer's disease.

Keywords: spoken discourse; microstructure; Alzheimer's disease; brain density; low socioeconomic status; low education level.

Introduction

Alzheimer's disease (AD) is an irreversible neurocognitive disorder characterized by progressive and degenerative cognitive impairment and widespread regional brain atrophy. Forgetfulness and memory impairment are the initial clinical signs of AD, which can affect episodic and semantic memory (Jahn, 2013). Episodic memory impairments have been shown to have a very high predictive value of AD (Edmonds et al., 2015; Ewers et al., 2012) and have consequently been the subject of many studies in AD. Language impairments have been identified as an early clinical manifestation of AD because the presence of language impairments is consistently reported not only in AD (Ahmed et al., 2013), but also in people with preclinical AD years before its diagnosis (Clark et al., 2009; Taler & Phillips, 2008). Impairments in several aspects of language production have been consistently reported in the lexical, semantic and pragmatic domains in the early phase of AD, extending to syntax and articulation with the progression of the disease (Szatloczki et al., 2015).

Spoken discourse is among the most complex tasks of oral communication because it requires the use and integration of different cognitive functions and language abilities to support the production of multiple combinations of ideas. According to the broad scientific consensus, discourse is defined as a component of language larger than an utterance or a sentence (Kong et al., 2016). In fact, discourse is the most elaborate manifestation of human expressive language (Ska et al., 2004). The study of expressive discourse is thus complex even in persons without neurological impairments, given that it can be modulated by demographic variables (e.g., age, gender, and education), cognitive variables (e.g., attention and executive functioning), and linguistic variables, such as the type of discourse assessed and the extracted measures (AbdulSabur et al., 2014). To date, over 536 measures of expressive discourse have been reported in the literature (Bryant et al., 2016). They can be grouped into two types: analysis using qualitative scales (e.g., grammatical form, presence of paraphasias) and quantification of micro- and macro-structural variables (Stark et al., 2021). Microstructural measures focus on the linguistic microstructure and allow for a detailed and often quantitative analysis of the different units within an utterance. The number of words per sentence and the average length of utterances are examples of variables commonly used. Macrostructural variables, on the other hand, allow us to situate the language in its context and to focus on the meaning of the utterances and the relationship between them. Discourse structure, cohesion, coherence, and informativeness are examples of macrostructural aspects. Micro- and macro-structural measures are often combined to provide a more complete portrait of the complexity of discourse skills (Marini et al., 2011).

Spoken discourse assessment and analysis are gaining widespread importance in clinical and research practices in post-stroke aphasia (Stark et al., 2021), and more recently in AD (e.g., Filiou et al., 2020; Mueller et al., 2018) because it allows the simultaneous assessment of several faculties, such as language, memory, executive functions, in a more ecological way than tests targeting these functions separately (Filiou et al., 2020). Linguistic discourse analysis assesses the relations between language abilities which are otherwise classically analyzed by discrete language measures (Prins & Bastiaanse, 2004). Therefore, it helps disentangle the underlying language aspects impaired in AD (Ahmed & Garrard, 2012). Although discourse offers the advantage of allowing to investigate all language domains in the same task, the scoping review of Filiou et al. (2020) showed that most studies have focused on one or two domains. Language deficits are widely recognized in AD and impairments in spoken discourse have been frequently reported in six different language domains: 1) speech rate; 2) structural and syntactic measures; 3) lexical measures; 4) morphological and inflectional measures; 5) semantic measures; and 6) measures of spontaneity and fluency disruptions. Among the most consistent results, individuals with AD would have a slower speech rate, and would produce fewer words (Petti et al., 2020) in terms of speech production compared to people without brain damage. According to a recent systematic review on verb processing, persons with AD tend to use simpler structures, but few grammatical errors (Williams et al., 2021) than people without brain damage. As for lexical access difficulties, they are more pronounced for words of lower lexical frequency, of shorter word length (e.g., Kavé & Goral, 2016), while there is also a lower richness of vocabulary, as measured by type-token ratio (Bucks et al., 2000), Honoré's index (Bucks et al., 2000; Fraser et al., 2016) and Brunet's index (Bucks et al., 2000). At the semantic content level, the most discriminant measures have been observed with information content and word finding delays (e.g., Nicholas et al., 1985), as early as the first stage of AD (e.g., Forbes-McKay & Venneri, 2005). Verbal fluency is also decreased in AD, with higher rates of repetition, modalization, hesitation, and unfilled pauses (Pistono et al., 2021). Pragmatic aspects have been less systematically reported, but people with AD tend to show a decrease in global coherence (Dijkstra et al., 2004) compared to people without brain damage, which has been positively correlated with the semantic and episodic performance (Brandão et al., 2013). Nonetheless, results are still inconsistent depending on several factors, including sample size, variables selected, variable extraction method and task used to elicit discourse production (Filiou et al., 2020; Slegers et al., 2018). Research on spoken discourse in AD and MCI would benefit from a more standardized and psychometrically sound assessment, such as the effort made in post-stroke aphasia (Stark et al., 2021, 2022), and from a multidimensional approach to have a more comprehensive understanding of discourse abilities (Filiou et al., 2020; Slegers et al., 2018).

As defined previously, discourse, also called connected speech, refers to the continuous production beyond the sentence level, which includes either unconstrained productions such as conversation, or more constrained productions such as personal narratives (i.e., ask a person to speak about a topic) and picture description (Armstrong, 2000). The most natural discourse genre is conversation, but the interaction with another speaker and the high inter-individual variability of spontaneous speech, inherent in a unique and personal complex cognitive task, complicates the analysis and the comparisons across participants. On the other hand, a single picture description task is a less natural discourse genre, but it has the advantage of being more predictable and is thus easier to evaluate with standardized measures (Mueller et al., 2018). Unsurprisingly, the single-picture description task has been the most used task in studies aiming at investigating connected speech abilities in Mild Cognitive Impairment (MCI) and AD (Filiou et al., 2020). The use of picture description has the advantage of reducing the demands on episodic memory because the story is visually presented to the participant (Duong et al., 2003). Although less adopted in previous studies in AD, the use of a sequence of actions has the advantage of requiring the participant to use more cohesive devices to establish the relationship between the different events of the story compared to a single-picture description task (Drummond et al., 2015). Interestingly, a study comparing a group of French-speaking people without brain injury and AD participants reported that discursive deficits were greater in a single-picture description task than in a multiple-picture task (Duong et al., 2005). One possible explanation is that the use of multiple pictures supports a better temporal organization of the story. The production of pauses has also been compared between sequential picture description and memory-based narratives in a group of persons with AD and a group of persons without brain injury (Pistono et al., 2019). More pauses were produced in sequential picture description in the AD group, and these were correlated with the lexical content index. On the other hand, pauses in the memory-based narratives were correlated with memory performance in the AD group. Sequential picture description has also been used in a study comparing the production of main concepts in people with AD (Kong et al., 2016). Presence, completeness, accuracy, and efficiency of producing main concepts were significantly lower in AD compared to people without brain injury. These previous findings support the importance of investigating sequential picture description in AD.

The role of sociodemographic and sociocultural characteristics on AD and spoken discourse

AD is the most prevalent neurodegenerative disease in the world, but the prevalence varies depending on the countries. According to a systematic review and meta-analysis (Prince et al., 2013), the prevalence of AD in Latin America was estimated to be 8.5% in individuals 60 years and older, which represents the highest rate in the world. Education level is among the environmental factors that could account for the high prevalence in Latin America. According to the Pan American Health Organization core indicators (PAHO, 2022), the mean education level of the population in North America (i.e., Canada and the United States of America) in 2018 was of 13.7 years, compared to 8.9 years in the Southern part of Latin America and 8.0 years in Brazil. Results regarding the effect of education on the risk of dementia and Alzheimer's disease were initially inconsistent, but education has been identified as a modifiable risk factor for dementia by the 2017 Lancet Commission (Livingston et al., 2020). Socioeconomic status (SES) is also very different between high-income countries and low-income and middle-income countries (LMIC). For instance, the mean gross national income per capita is nearly nine times higher in North America compared to Brazil, which was respectively $68189 US and $7720 in 2021 (PAHO, 2022). Although dementia prevalence is higher in LMIC than in high-income countries, most studies conducted to date have been conducted in higher-income countries. The same bias occurs in relation to education, which is very much linked to SES. Studies have reported an increase in neurocognitive processing as a function of higher educational levels (Cotrena et al., 2016). Borelli et al. (2022) investigated the prevalence of subjective cognitive decline (SCD) in Brazil. They reported that SCD was most strongly associated with Brown/Pardo and Black races, but also with dementia-modifiable risk factors such as hearing loss, low education, and psychological distress. Altogether, this suggests that it is crucial to pursue the effort to conduct studies on people from LMIC as the results obtained from high-income countries may not be generalizable.

Regarding discourse abilities, knowledge of the topic (Shapiro, 2004) and of discourse genre (narrative vs. expository; Clinton et al., 2020; Mar et al., 2021), literacy abilities (Mellard et al., 2010), level of education (Mackenzie, 2000), age (Mackenzie, 2000; Martin et al., 2018) and reading/writing habits (Martin et al., 2012) are variables that can influence discourse processing. Studies in post-stroke aphasia have already associated SES with the severity of linguistic and cognitive impairment and with patterns of recovery. For example, Song et al. (2017) conducted a multinomial logistic model analysis which showed that low educational level and manual laboring have a more significant impact on the functional outcome three months following an ischemic stroke than does low-income level. Despite the relevance of studies on the impact of low education level and low SES, such studies are still very scarce in people with AD. Moreover, according to a scoping review on the methodology used to assess discourse production in MCI and AD (Filiou et al., 2020), over 40% of the studies were conducted in English-speaking populations, which reflects a substantial gap for the other languages, since the language spoken can have an impact on discourse abilities (Mehler, 1994). Similarly, most studies on narrative comprehension have been conducted with adults from high-income countries, where education levels are higher than in LMIC according to the education index of the Human Development Reports (United Nations Development Programme, 2020). Furthermore, some studies conducted in high-income countries have been conducted in people with AD with higher levels of education (e.g., Drummond et al., 2015). Since education and SES relate to cognitive (including linguistic) performance, those studies may not be generalizable for people with lower levels of education and SES from LMIC. This lack of linguistic diversity constitutes a barrier towards the discovery of globally equitable tests and measures markers of brain healt early identification of neurodegenerative disorders such as AD s AD (García et al., 2023).

Structural correlates of AD and spoken discourse considering educational level and SES

According to a meta-analysis of voxel-based morphometry (VBM) studies in AD (Chapleau et al., 2016), the classical early pattern of atrophy in AD starts in the hippocampus bilaterally and in the posterior medial temporal regions, extending later to other cortical areas. Limbic regions and specifically the left parahippocampal gyrus and left posterior cingulate gyrus (Wang et al., 2015) as well as the bilateral hippocampus/amygdala complex (Frisoni, 2002) appear to be most affected by AD. Several factors other than AD can also influence cortical density, such as education level (Richards & Sacker, 2003), socioeconomic status and literacy (Manly et al., 2005). Education and richness of cognitively stimulating life experiences have been shown to develop a cognitive reserve, which is supported by an increase neurogenesis in the dentate gyrus, an increase neuronal plasticity, and may be associated with increased cortical density (Stern et al., 1995). In fact, several studies demonstrate the implication of the level of education and SES in the constitution of cognitive reserve and by extension on cortical density (Stern, 2009). It is important to acknowledge that SES is a complex proxy of cognitive reserve intrinsically related to other measures of cognitive reserve, such as education, as already mentioned, and bilingualism (Bialystok, 2021), among others. Therefore, education or SES are more difficult to examine as isolated factors. However, education itself has been shown to be a determinant factor of brain size and volume in typical adulthood (Kim et al., 2023). Early-life exposure to high education has been proposed to have a neuroprotective effect on the aging brain against cortical thinning (Chen et al., 2019; Walhovd et al., 2023), as well as in postponing dementia (Fratiglioni & Wang, 2007). Furthermore, the neuroprotective effect of education against cortical thinning of the aging brain has shown a lifetime effect. For example, Steffener (2021) demonstrated an effect of higher education in gray matter maintenance until later ages, while this protection declined year by year in late life in those individuals with greater levels of education. Thus, the impact of education on a lifespan, mainly in later ages, needs to be more fully addressed. Finally, sex differences have also been observed in terms of brain volume. Compared to males, greater grey matter volume has been reported in females (Peng et al., 2016). Similarly, cortical thickness has been reported to be thinner in males than in females, but the differences due to sex were reduced in MCI and AD groups (Sangha et al., 2021). This is particularly important considering that evidence suggests the prevalence of AD in females as compared to males (Fratiglioni et al., 1997).

So far, only a limited number of studies have focused on the neural correlates of language impairments in AD (Szatloczki et al., 2015). Previous studies have focused on episodic memory with limited studies looking at language. Although changes in neural networks supporting language processing have been reported (Mascali et al., 2018; Pistono et al., 2021), correlations between the degree of connectivity in the language network (perisylvian cortex mainly) and language tasks are less common. Among the few, a recent study showed that participants with AD performed similarly to participants without neurological impairment in complex semantic and pragmatic tasks, despite showing a typical pattern of temporo-parietal atrophy attributed to AD (Luzzi et al., 2020). Mascali and colleagues (2018) did not find correlations between the brain activation of the language-related areas and language tasks in a group of participants with mild AD, whereas Pistono and colleagues (2021) found that increased connectivity along the left perisylvian cortices, more specifically between the inferior frontal gyrus and the superior temporal gyrus, was correlated with the performance in a sentence production task (i.e, production of a sentence using given words). This evidence shows that a compensation in language abilities (at least at the macrostructural level) may exist, even if neural changes take place in the population with AD. Spoken discourse tasks require the combination of different aspects of language at the same time, at the general performance level (e.g., pragmatics) but also at the microstructural level (e.g., syntactic variations), which makes them ideal to identify subtle changes that otherwise would pass unnoticed until more severe impairments appear. Most importantly, these behavioral changes have not been associated with brain changes, which leaves unanswered the question of whether this association could be a potential marker of AD.

Purpose

The present study aims to extend our knowledge of the impact of AD on spoken discourse abilities in people with low levels of education and middle-low to low SES. Considering the underrepresentation of languages others than English in research of discourse abilities in AD, it is critical to report on non-dominant languages in order to have a better understanding of the linguistics specificities to minimize the global inequities. Thus, we aim to fill the gap by reporting on a group of unilingual Brazilian Portuguese speakers. The objectives are twofold. First, we examine whether there are differences on the microstructural characteristics of spoken discourse between women with AD and women without brain injury (WWBI). Spoken discourse assessment is relatively easy to do, cost-effective, and could improve the detection of AD in countries such as Brazil where brain imaging is less easily available than in other countries. Based on recent systematic (Slegers et al., 2018; Williams et al., 2021) and scoping (Filiou et al., 2020) reviews on connected speech in participants with AD, we hypothesize that differences can be observed at the lexical and the syntactic level, as well as in the amount of production. Second, we intend to explore the association between the microstructural measures of spoken discourse and their structural correlates in grey matter (GM). Previous studies have not yielded strong conclusions on the impact of AD-related atrophy on discourse measures. The present exploratory study will help to develop specific hypothesis which will be tested in future research.

Method

Participants

The study was approved by the Research Ethics Committee under report number 560.073, CAAE registry number 21006913.0.0000.5336. Participation in the study was voluntary, and participants provided written informed consent before joining the study. Nineteen participants were included in the study. The demographic and clinical variables of both groups are presented in Table 1. All participants were native Brazilian Portuguese speakers and did not speak other languages. They were recruited at community centers, in an urban context in the southernmost state of Brazil. Participants were from low to middle-to-low socioeconomic status.

Originally, both males and females were recruited for the study. A flow diagram of the progress through the phases of the study (that is, enrolment, group allocation, and data analysis) is reported in Supplementary Material 1. As reported in the diagram, a large majority of women were recruited. Considering the potential role of sex on both the behavioral and neuroimaging results, we decided to only report data from female participants. Thus, the group of people diagnosed with AD consisted of nine female patients who attended the neurology service at a hospital affiliated to the university where the study was registered. They were diagnosed at a mild AD stage (level 1) according to the Clinical Dementia Rating (Morris, 1993) completed by a neurologist. Exclusion criteria consisted of 1) a history of psychiatric disorder; 2) severe visual and auditory perceptual deficit; 3) no previous neurological disorders (e.g., stroke, tumor, epilepsy, brain injury); 4) no current or previous history of substance abuse, or dependence (alcohol, drugs, and benzodiazepines); and 5) left-handedness or ambidexterity which was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

The WWBI group consisted of 11 female healthy participants recruited at community centers. In addition to the exclusion criteria used with AD patients, WWBI were also excluded if their score on the Mini-Mental State Examination (MMSE) was lower than the age and educational specific cut-off score adapted for the Brazilian population (Brucki et al., 2003): illiterate = 20 points; 1-4 years of education = 25 points; 5-8 years of education = 26.5 points; 9-11 years of education = 28 points; $\geq$ 11years of education = 29 points).

Materials and procedures

Sociodemographic questionnaires

As in our previous studies (Schneider et al., 2021, 2022), participants were also asked to complete the *Questionário de condição social,* taken from *Associação Brasileira de Empresa e Pesquisa* (Abep, 2015) (https://www.abep.org/criterio-brasil), to measure the SES. The score is calculated based on household characteristics, the education level of the head of household, and consumer goods and amenities. It establishes the following cut-off points: lower SES = 0 to 16; middle = 17 to 28; upper middle = 29 to 44; upper = 45 to 100.

Moreover, participants completed a questionnaire (Pawlowski et al., 2012) measuring reading and writing habits (RWH). Participants evaluated their frequency of reading different types of printed and digital material, such as magazines, newspapers, books, social media, and the frequency of writing notes, text messages, literary and/or non-literary texts, both weekly. Frequency ratings of both reading and writing habits were scored using a four-point scale for each type of material: daily (4 points); a few days a week (3 points); once a week (2 points); rarely (1 point), and never (0 points), with a maximum score of 16 points for each modality (reading and writing).

Neuropsychological assessment

All participants took part in a larger study aiming to map age and dementia-related changes in language processing. The *episodic memory task* from the *Bateria de Avaliação da Linguagem no Envelhecimento* (BALE; Hübner et al., 2019) consists of identifying and learning 16 figures from different semantic categories of nouns, grouped in four charts with four items each, with three recalls: two times free immediate recall plus cued immediate recall and a 20-minute delayed recall, while *working memory* was evaluated with the WAIS-III Digit Span and Backward Digit Span subtests (Wechsler, 1997). The semantic knowledge task consists of completing and explaining the meaning of three proverbs (6 points) and explaining the meaning of three metaphors (3 points), for a maximum score of 9. The *semantic association task* is composed of 12 sets of pictures, each one containing four stimuli: a prime picture on top and three possible targets below it. Participants point

Commenté [KM1]: I looked at your 2022 paper, but make sure this is correct. To respond to comment 3 of reviewer 2

Commenté [li2R1]: I reworded, please see if it is clear.

Commenté [KM3R1]: Why two times?

Commenté [KM4R1]: One time free immediate recall, one time cued immediate recall and one 20-minute delayed recall?

Commenté [li5R1]: No, one time free + cued; then another free + cued; then one 20 min later to the target picture, among the three options, that has the closest semantic relation to the prime one. The maximum score for this task is 24, with a maximum of two points for each association trial (two points for each correct association followed by the right explanation, one point for the correct association but without the expected explanation; no points for an incorrect association between the two chosen pictures). The *naming task* consists of 60 black and white drawings, balanced regarding animate versus inanimate and high versus low-frequency items, presented in groups of four in an A4 sheet. The total score for this task is 60, one point for each correct answer. The *verbal semantic fluency task* consists of generating words for the animal category for one minute, while the *verbal phonemic fluency task* consists of saying as many words as possible for one minute using the phoneme /p/. These tasks are subtasks of BALE (Hübner et al., 2019).

Discourse assessment

Spoken discourse was elicited with two tasks taken from BALE (Hübner et al., 2019): (a) a picture sequence task and (b) a free discourse task. The *picture sequence task* is known as "The dog story". Participants were asked to tell the story based on seven scenes, according to the following instruction: "I will show you a story with scenes. Each scene is a moment in the story, which has a beginning, middle, and end. I will ask you to take a good look at the scenes and try to understand the story. Then, I am going to ask you to tell me this story as if you were going to tell it to a friend. Are you ready? Can we start?". The pictures were presented in the correct sequence and remained in front of the participant so that s/he could observe them while telling the story. Participants were given time to observe the scenes and, if necessary, the instruction was repeated. There was no time limit for the accomplishment of the task. In the *free discourse task*, participants were asked to tell a funny story, according to the following instruction: "I would like you to tell me a funny story that happened to you, or that you witnessed, or that you were told. It cannot be a joke". Completion of the task had no time limit.

MRI protocol

One high-resolution three-dimensional (3D) T1-weighted scan was acquired on a GE Healthcare 3.0T HDxt MRI scanner using an 8-channel skull coil. A Magnetization Prepared Rapid Gradient Echo (MP-RAGE) sequence was acquired using these parameters: TR = 6272 msec, TE = 2255 msec, TI = 500 msec, voxel size = 1x1x1 mm3, matrix = 240 x 240, 196 slices.

Preprocessing

Discourse transcription and data extraction

All discourse samples were audio-recorded for later transcription. Transcriptions were made by two independent researchers, and discrepancies between the two were resolved through discussion. Transcriptions were segmented into utterances, in which a full stop marked the end of each utterance, as proposed by Thompson et al. (2012), who define utterances as being a group of words expressing a complete thought. Linguistic metrics were obtained from the two narratives combined using the NILC-Metrix software (Leal et al., 2022), which is based on Coh-Metrix (Aluísio, Sandra Maria et al., 2016; Graesser et al., 2004, 2011; Graesser & McNamara, 2011). The software automatically generates 200 language metrics, including lexical and syntactic information, readability and psycholinguistic measures, and metrics of referential and semantic cohesion. First, all the measures related to the standard deviation (n = 10), minimum (n = 7) and maximum (n = 7) values, measures (n = 24) subdivided for a more refined analysis (e.g., sentences with five clauses, sentences with four clauses, sentences with one clause…) were excluded from the analysis. Then, using the systematic review of Filiou et al. (2020), we reviewed all remaining measures and excluded the less reported measures (e.g., grammatical particles ratio, ratios between subclasses of word categories, etc.). Finally, the variance of the remaining 92 variables was then calculated, and all measures with a variance of 0 were excluded. Thus, of the initial 200 variables, 171 variables were excluded, which led to a total of 29 variables analyzed with NILC-Metrix.

Briefly, we analyzed nine different categories of measures: connector measures (connector ratio), descriptive measures (sentences, words per sentence, words), lexical diversity (preposition diversity, pronoun diversity, relative clauses, indicative present ratio, noun diversity, type-to-token ratio, content word diversity), psycholinguistic measures (concreteness mean, imageability mean, age of acquisition mean, familiarity mean), readability measures (Brunet index, Honore's index, Flesch index), syntax complexity (Frazier, Yngve), temporal lexicon (verbal time mood diversity), word frequency (content word frequency), word morphosyntactic information (verbs, noun ratio, inflected verbs, pronoun ratio, infinitive verbs). Each feature is explained in detail, in Brazilian Portuguese, on the NILC-Metrix website (http://fw.nilc.icmc.usp.br:23380/nilcmetrix).

MRI preprocessing

First, the raw DICOM scans were converted into the Neuroimaging Informatics Technology Initiative format (nifti) using MRIcroGL (https://www.nitrc.org/projects/mricrogl/) (Rorden & Brett, 2000). Voxel-based morphometry (VBM) pre-processing was performed using the default settings of the Computational Anatomy Toolbox (CAT12, version 12, https://www.nitrc.org/projects/mricrogl/) (Rorden & Brett, 2000). Briefly, a spatially adaptive non-local means denoising filter (Manjón et al., 2010) is applied and all 3D T1-weighted MRI scans are normalized using an affine followed by non-linear registration, corrected for bias field in homogeneities, and then segmented into grey matter, white matter, and cerebrospinal fluid (Ashburner & Friston, 2005). Then, we used the Diffeomorphic Anatomic Registration Through Exponentiated Lie algebra algorithm (DARTEL; Ashburner, 2007) to normalize the segmented scans into a standard MNI space. The resulting images were visually inspected one by one using MRIcroGL to exclude macroscopic segmentation errors. Finally, all images obtained from the segmentation of normalized images were smoothed using the full-width-half-maximum (FWHM) Gaussian kernel of 12 mm.) (Rorden & Brett, 2000).

Statistical analyses

Behavioral analyses

Statistical analysis was conducted using the Statistical Package for the Social Science (SPSS) version 28.0.1.0 statistical software. An independent samples t-test was performed on the 29 remaining variables to highlight the variables that were significantly different in the AD compared to the WWBI group. To avoid the inflation of Type I error rate, a Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995) was applied for the 29 comparisons, using a false discovery rate of 25%.

Neuroimaging analyses

In the first step, whole-brain statistical analyses were performed in SPM12 using the smoothed GM maps to assess whole-brain effects. Second-level general linear models were specified including the two groups (AD and WWBI) and total intracranial volume (TIV) as covariate of no interest. In a second step, we performed a regression model, which included both the AD and the WWBI groups, using the whole brain GM maps as well as the scores of the discursive measures as a dependent outcome and TIV as covariate of no interest, to identify brain regions where GM density reductions were associated with discursive performance. For both analyses, a family-wise error (FWE) correction at $p < .05$ at the cluster level was applied, using an arbitrary cluster-forming uncorrected threshold of $p < .001$. Additionally, effect sizes for significant comparisons were calculated using the T-statistics (t) and the degrees of freedom (df) in the $\sqrt[2]{t^2/(t^2+df))}$ (Lukic et al., 2021). Anatomical labeling was performed at Neuromorphometrics, Inc., following the methods described in Caviness et al.(1999)

Results

Participants

Table 1 presents demographic information and mean neuropsychological evaluation scores for both AD and WWBI groups. Both groups of participants were matched for age, education, and socioeconomic status as well as reading habits (all $p > .05$; see Table 1). However, a significant difference was present regarding writing habits (t = - 2.38, *p* = .030), for which the WWBI group reported to have more writing habits than the AD group. Regarding the neuropsychological assessment, the most significant differences were observed between the two groups on the MMSE (t = - 5.950, *p* < .001) and on all episodic memory subtasks except for episodic memory cued (t = - .53, *p* = .959), for which women diagnosed with AD had a lower performance than WWBI. Significant differences were also observed on the Trail Making Test (Version A: t = 3.07, *p* = .007; Version B: t = 3.00, *p* = .010), but there were no differences in the digit span tasks (all *p* > .05; see Table 1). Differences were also observed between the two groups on the semantic verbal fluency (t = - 5.15, *p* < .001), phonemic verbal fluency (t = - 2.29, *p* = .038), and on the naming task (t = - 4.03, *p* = .001), for which women with AD had a lower performance than WWBI. Significant differences were also observed on semantic association (U = 70.00, *p* = .043), but not on the semantic knowledge tasks (composed by the proverbs and metaphors subtasks) (*p* > 0.05; see Table 1).

Discourse results

Mean and standard deviations (mean ± SD), as well as the range for each group, are reported in Supplementary Table 2 in addition to the statistical values of the tests. Only six variables showed a significant difference between the two groups after the Benjamini-Hochberg FDR correction. Figure 1 represents the variability of these variables. Namely, compared to the WWBI group, the AD group produced fewer sentences (t = - 2.92, *p* = .010), fewer words (t = - 2.54, *p* = .021), and a lower verbal time moods diversity t = - 3.00, *p* = .008), whereas they produced a greater diversity of prepositions (t = - 2.39, p = .029) and of pronouns (t = 2.35, *p* = .031) and a greater lexical richness, with a mean Brunet's index lower than in the WWBI group (t = - 2.35, *p* = .031).

Imaging results

Identification of grey matter density differences between groups

VBM analyses were computed to identify grey matter density differences between the groups. Total intracranial volume was included as nuisance covariables to account for interindividual differences. Significant differences are depicted in Figure 2. Women with AD compared to WWBI showed a reduction in grey matter density in the left and right anterior cingulate gyrus, left hippocampus, right hippocampus, and bilaterally in the inferior temporal gyrus. No regions showed significant greater cortical density in the AD group compared to the WWBI group.

Linear regression-based analysis of discursive variables

Regression-based analyses were computed, after controlling for TIV, between regional GM volume as measured by whole-brain VBM and the discourse measures. The anatomical labeling of the clusters is listed in Table 2. One significant cluster located in the left parahippocampal gyrus (MNI 152 coordinates -24 -20 -33) was significantly and positively correlated with the number of words produced ($T = 5.39$; $k = 842$) and the number of sentences ($T = 6.11$; $k = 441$). Grey matter density was also positively correlated with verbal time mood diversity with a cluster located in the left pallidum/amygdala gyrus (MNI 152 coordinates -18 -4 -9; $T = 4.20$; $k = 382$) as well as with a cluster located in the anterior cingulate gyrus (MNI 152 coordinates 3 46 3; $T = 4.58$, $k = 313$) (Figure 3).

Discussion

This study first aimed to examine whether there are differences on the microstructural characteristics of spoken discourse between women diagnosed with AD and WWBI, in a context of low level of education and low-to-middle SES. The AD group produced fewer sentences and fewer words, and a lower verbal time moods diversity. On the other hand, they produced a higher diversity of prepositions and pronouns, and showed a greater lexical richness, as shown by a lower Brunet index. Second, we identified a reduction in grey matter density in the left and right anterior cingulate gyrus, left hippocampus, right hippocampus, and bilaterally in the inferior temporal gyrus in women with AD compared to WWBI. Third, we aimed to explore the association between the microstructural measures of spoken discourse and their structural differences in GM. Number of words and sentences produced was positively associated with grey matter density in the left parahippocampal gyrus, whereas verbal time mood diversity was associated with grey matter density in the left pallidum/amygdala gyrus and in the anterior cingulate gyrus. We grouped the discussion following these three aims.

Microstructural characteristics of spoken discourse

The present results extend what is already known in populations form higher SES background. Consistent with previous evidence (Petti et al., 2020), the AD group produced fewer words than the WWBI group in the discourse tasks. Likewise, significant differences in word retrieval-based neuropsychological tests were also found between the AD group and the WWBI. Consistent with previous evidence reporting a decreased verbal fluency in AD, with higher rates of repetition, modalization, hesitation, and unfilled pauses (Pistono et al., 2021), lower performances were obtained in the AD group as compared to the WWBI group in the phonemic and semantic verbal fluency. Lower performance by the AD group was also observed in tasks involving semantic memory (naming task and semantic association task) and in episodic memory (verbal learning task). In fact, significant differences found in language-based neuropsychological tests in our samples reveal a lower performance in word and content retrieval tasks, which indicates that this underlying impairment leads to a lesser production of items. These findings may indicate limited access to word meanings, and difficulty in lexical retrieval and word generation in AD, which may limit the length of the speech samples in this population. Previous evidence has suggested that lexical retrieval impairments observed in written picture description discourse could be a sensitive marker of AD, even in the early stage (Forbes et al., 2004; Pekkala et al., 2013). However, the use of written discourse in persons with lower levels of education is more challenging as some might not have learned how to write. The present result suggests that similar results can be obtained using a spoken discourse task and that it could be an early indicator of AD in populations with lower levels of education. Alternatively, reduced memory skills observed in AD could also account for lower performance on retrieval tasks. The differentiation between language and memory impairments is difficult since the two are interwoven (Mueller et al., 2018), and should be further studied.

In a review with meta-analysis (Kavé & Goral, 2018), conflicting evidence has been reported regarding lexical richness. By definition, lexical richness seems to be operationalized as a measure of proficiency and vocabulary knowledge (Jarvis, 2013) which seems to increase with age because of experience and world knowledge (Huilt et al., 2011). The present results showed that the AD group produced a greater lexical richness, with a mean Brunet's index lower than in the WWBI group. In contrast, lower richness of vocabulary, as measured by type-token ratio, Honoré's index and Brunet's index, has been reported in AD (e.g., Bucks et al., 2000). Fraser et al. (2016) found that Honoré's statistic was lower for adults with AD than controls in the descriptive discourse task using cookie theft samples from a group of 167 adults with AD. Honoré's statistics was part of the semantic factor derived from the factor analysis made to reduce the top 50 features extracted from the discourse samples. However, none of the other measures of lexical richness, which included Brunet's index and type-token ratio, were in the top 50 factors. Similarly, no significant difference in terms of lexical richness (i.e., moving-average type-token ratio) was found in AD compared to persons without brain damage (Cho et al., 2022), which could point out that the complexity of lexical richness may be less sensitive in this population compared to other measures of a more structural nature. In the same vein, it could be debated at which point it might serve as an early sign of AD (e.g., Kavé, Goral, 2016).

Lexical content has also been examined through proportions of different parts of speech such as proportions of pronouns, nouns, adjectives, and verbs. The AD group produced a greater diversity of prepositions and of pronouns than the WWBI group, as reported in previous studies (Almor et al., 1999; Bucks et al., 2000; Fraser et al., 2016; Lindsay et al., 2021). One potential explanation of a higher recurrence to prepositions and repeated pronouns is that it may indicate a difficulty to access content words and adequate references that could substitute the pronouns, which may lead to ambiguity due to the use of vague pronouns referring to an element in the text, as well as an emptier discourse (Lindsay et al., 2021). The establishment and maintenance of references are central in language processing since much of what we talk about refers to entities in the word. In this aspect, pronouns are vital, and they need to clearly point to elements in or outside the linguistic context and must be kept in mind by the speaker, while being made clear to the listener – this shows its intrinsic relation with memory systems. The adequate use of pronouns is necessary to promote discourse coherence, which is impaired in AD (Drummond et al., 2015; Toledo et al., 2018). Another potential explanation for the higher use of prepositions and pronouns is that the nature of this difficulty may rely on a perspective-taking difficulty, specifically on taking the hearer's perspective. Bittner and collaborators (2022) analyzed nine types of pronouns, including, for example, pronouns with reference to persons and objects, the impersonal pronoun *man* in German ("one", in English), and the propositional pronoun *das* (this/that) in semi-spontaneous biographical interviews. They reported a correlation between the use of these pronouns and declines in elaborative and evaluative information, that is, information the listener would have benefitted from to create a better model of discourse. Interestingly, changes in pronoun use may be detectable a decade before the clinical diagnosis of AD (Bittner et al., 2022). Further studies should investigate the generation of pronouns in other types of discourse tasks, as well as the impact of impairment on specific types of pronouns, to benefit clinical applications.

According to recent systematic reviews (Filiou et al., 2020; Slegers et al., 2018), morphological and inflectional measures as well as structural and syntactic measures should be observed when investigating discourse in AD. While Kavé and Levy (2003) did not find differences between AD and age-matched control participants in syntactic (e.g., production of independent and declarative clauses) and morphological aspects (e.g., word inflection, verb formation), others have reported difficulties in the production of tense, aspect, agreement, and mood in AD (Fyndanis et al., 2018; Roumpea et al., 2019). In the present study, neither of the syntactic nor the morphological measures were found significantly different between the two groups, which is consistent with the systematic review of Williams et al. (Williams et al., 2021) who reported a relative preservation of syntactic and grammatical abilities. Nonetheless, lower verbal time mood diversity was observed in the AD group compared to the WWBI. According to the NILC-Metrix classification, verbal time mood diversity is a measure of temporal lexicon. The present result could indicate impaired use of syntactic moods, due to a reduced ability to select the proper mood according to the idea to be elicited. Fyndanis et al. (2018) explored subject–verb agreement, tense/time reference, and mood production in sentence completion tasks in two highly inflected languages (i.e., Greek and Italian) to assess whether verb-related morphosyntactic production is (selectively) impaired in AD. Both Greek and Italian participants with AD performed worse than the control group. Moreover, the AD groups revealed different patterns of morphosyntactic production (Greek: agreement/mood > time reference; Italian: Agreement > Time Reference > Mood). Past reference was more impaired than future reference. They conclude that there are syntactic aspects impaired in AD, and that the different patterns observed in the two languages may be partly attributable to the different form these languages encode mood. These results support the importance of studying cross-linguistic patterns of morphosyntactic impairment in dementia and point to the necessity of expanding the testing of these features to a variety of oral discourse production tasks and languages.

Structural correlates of AD

Synaptic loss and a consequent brain focal atrophy represent a hallmark of AD and are generally associated with cognitive impairment (Scheff et al., 2011). Consistent with previous evidence in people with higher levels of education and SES (Chapleau et al., 2016; Frisoni, 2002; Wang et al., 2015), women with AD compared to WWBI women showed a reduction in grey matter density in the areas comprising the left and right anterior cingulate gyrus, left and right hippocampus, and bilaterally in the inferior temporal gyrus. In their meta-analysis of VBM studies on AD, Chapleau and collaborators (2016) proposed a classical early pattern of atrophy in AD which starts at the hippocampus bilaterally and in posterior medial temporal regions, extending after to other cortical areas. Atrophy in the hippocampus bilaterally has widely been known as a marker of AD (Dubois et al., 2015; Uysal & Ozturk, 2020). Yet atrophy in the right posterior cingulate cortex/precuneus has also been reported in AD patients when compared to the behavioral variant of frontotemporal dementia by Smith et al. (2002). Significant atrophy in the cingulate has been reported in AD in all four cingulate regions (rostral anterior, caudal anterior, posterior cingulate gyrus and retrosplenial cortex), with higher atrophy in the posterior cingulate gyrus as compared to the other three areas (Jones et al., 2006). Thus, our results are consistent with the literature which reports cortical atrophy in this region, although it is more often the posterior (and not anterior) cingulate gyrus that is reported (Leube et al., 2008). Further studies should analyze the possible effect of sociodemographic aspects, such as SES and education, in the specific participation of posterior versus anterior areas in the cingulate gyrus. Jones and colleagues (2006) suggest that detecting and monitoring cingulate regions atrophy may provide insights into the history of familial AD and may support the search for diagnostic markers of early AD. Finally, atrophy in the inferior temporal gyrus bilaterally may be particularly affected in less educated populations. In fact, Busatto et al. (2003) conducted a study like the present study with two groups of 14 participants with a low level of education (on average 9 years) recruited in Brazil. They reported, as in the present study, atrophy in the inferior temporal gyrus bilaterally, which could support the hypothesis that this area is specific to less educated populations. It would be interesting to explore this hypothesis in the future.

Structural correlates of spoken discourse

When it comes to the association between brain density and linguistic performance, the linear regression-based analyses of discourse variables associated with brain volume showed some clusters relating the brain to language processing. First, the left parahippocampal gyrus, significantly and positively correlated with the number of words and sentences produced. Labache et al. (2019) reported that the left parahippocampal gyrus is implicated in word and sentence production using a model of task-induced activation mapping, comparing the activation of words versus sentences. Conversely, it has been also observed in language generation tasks (Crosson et al., 2001), and implicated in memory functions as analyzed by a study on epilepsy using tractography (Yogarajah et al., 2008). The role of the parahippocampal gyrus in cognition needs to be more fully addressed, as suggested by Aminoff et al. (2013). The authors propose that, besides being associated to cognitive processes including visuospatial processing and episodic memory, this region would integrate a network which processes contextual associations, which underly several higher-level cognitive processes. In this sense, word and sentence generation would be crucial to elaborate associations, linking thoughts and language, to convey and understand oral (and possibly written) messages.

Second, verbal time mood diversity was positively correlated with a cluster located in the left pallidum/amygdala gyrus, as well as with a cluster located in the anterior cingulate gyrus. Limbic regions have been reported to have less grey matter density in the population with AD (specifically the left parahippocampal gyrus and the left posterior cingulate gyrus) (Wang et al., 2015). These areas belong to the Default Mode Network, whose functions include monitoring of online tasks, memory retrieval and attention. Lack of accuracy in verbal time mood assignation may just be one of the multiple expressions that atrophy in these brain areas may elicit. Similarly, other limbic regions (left pallidum/amygdala gyrus) shown to present atrophy in AD (Frisoni, 2002) were also implicated in verbal time mood diversity. The nature of the recruitment of syntactic, semantic, and contextual aspects in oral discourse production should be better investigated in future studies, to disentangle each of these components and contribute to preventive diagnoses and language intervention.

Importance of investigating AD from an equitable perspective

Taken together, the present results contribute to enlarging the reduced body of literature on the relation between oral discourse production and brain density in AD, including the perspective of a low-to-middle SES population, in a language with features such as rich morphology (as opposite to most of studies of AD carried out in English-speaking samples). Moreover, it shows the relevance of studies on the discourse level, since spoken discourse recruits the simultaneous combination of different linguistic and cognitive aspects, which makes it a potential tool to detect subtle changes already on the first stages of cognitive decline or dementia. Our study suggests the necessity of further studies combining the impact of microlinguistic aspects of oral discourse production as a function of task typology (testing other types of oral discourse elicitation), educational level (Richards & Sacker, 2003), and socioeconomic status and literacy (Manly et al., 2005) in cortical density in AD. The concept of cognitive reserve driven by education has been shown in samples with a variety of education and literacy background (Zhu et al., 2021). Our results suggest furthermore that the impact of AD in people with lower education and resource access can manifest in more subtle ways, which may not be detected by standard tools in this type of population. Education and literacy may function as compensation in cognitive (including linguistic) functioning for brain regions atrophy linked to AD, which represents an interesting area of study and may have implications for clinicians and social policymakers. The present study also contributes to the urgent global call of action to increase the linguistic and cultural diversity in the investigation of neurocognitive disorders, given the preponderance of studies conducted on English speakers in the literature (García et al., 2023). The present study is a first step to help reducing the global inequities across developing countries, such as Brazil, by collecting data in an under-represented language (i.e. Brazilian Portuguese) and by improving our knowledge of the impact of AD on spoken discourse in languages other than English. As members of the International Network for Cross-Linguistic Research on Brain Health, better known as Include (https://include-network.com), we aim to contribute to the generation of cross-linguistic markers able to differentiate between normal aging and the various neurodegenerative diseases using cost-effective language assessments, such as spoken discourse, which is critical to reduce the global inequities for the assessment of neurodegenerative diseases.

Limitations

The reduced number of participants in each group makes the conclusions exploratory, especially in terms of brain data. The small sample size may have contributed to reduced statistical power, which may have led to the failure in detecting significant results across the statistical tests in the VBM analysis (Lorca-Puls et al., 2018). Also, the fact that only women integrate the groups does not allow the generalization to men. However, studies with aging populations tend to include more women as compared to men due to the higher proportion of women of advancing age (United Nations, Department of Economic and Social Affairs, Population Division, 2019). Further studies should include larger samples of both sexes, also including higher SES and educational level groups to compare performance both at the behavioral and brain levels. Furthermore, it would be interesting to analyze other oral discourse tasks, such as procedural and auto-biographic discourse, as they may rely on different types of memory and production processes, to correlate with the data generated in this study, which included a narrative based on a sequence of pictures and the production of a funny story.

Conclusion

This study contributes to the existing body of evidence regarding microstructural aspects in discourse production by comparing the performance of older adults diagnosed with AD to that of WWBI. Moreover, it adds to the literature on understudied languages, Brazilian Portuguese in this case, and brings important contributions regarding the relation between brain density and oral discourse production in AD, a field to be further investigated, giving support to further comparative studies with the same population, or other clinical groups with cognitive decline or dementia, such as MCI and Primary Progressive Aphasia (PPA). Previous studies have not yielded strong conclusions on the impact of AD-related atrophy on discourse measures. The present exploratory study supports the development of specific hypotheses to be tested in future research. Furthermore, this study highlights the importance of taking into consideration sociodemographic profiles of participants, such as education, and SES, as important variables influencing the performance in oral discourse production, more specifically to what concerns the microlinguistic level and its relation to brain density, with implications for clinicians, physicians and public health and education policymakers.

Acknowledgments

We first would like to thank the participants and their families for their time. We also would like to thank Gislaine Machado Jerônimo, Anderson Dick Smidarle, Ellen Siqueira and Bruna Tessaro for their support in data collection and organization.

Data Availability Statement

The dataset generated during and analyzed during the current study is available from the corresponding author on reasonable request.

Funding

This study was financially supported by grants received by L.C.H. - CNPq (National Council of Technologic and Scientific Development) Universal grants no. 479989/2013-3 and 4524362508342994 – 28/2018, and grants as productivity researcher; *Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul* (FAPERGS) - Program for Internationalization of Graduate Education, grant no. 0429-2551/14-5; and CAPES (Coordination of Superior Level Staff Improvement). B.L.C.M. held a CNPq doctoral scholarship #140436/2018-9. A.O.G. holds a doctoral scholarship from Fonds de recherche Québec-Santé. H.de P. received a PREMIER grant from Université de Montréal for a research summer internship.

References

AbdulSabur, N. Y., Xu, Y., Liu, S., Chow, H. M., Baxter, M., Carson, J., & Braun, A. R. (2014). Neural correlates and network connectivity underlying narrative production and comprehension : A combined fMRI and PET study. *Cortex*, *57*, 107-127. https://doi.org/10.1016/j.cortex.2014.01.017

Ahmed, S., & Garrard, P. (2012). Spoken discourse in Alzheimer' disease : A review. *Linguistica*, *52*(1), 9-25. https://doi.org/10.4312/linguistica.52.1.9-25

Ahmed, S., Haigh, A.-M. F., de Jager, C. A., & Garrard, P. (2013). Connected speech as a marker of disease progression in autopsy-proven Alzheimer's disease. *Brain*, *136*(12), 3727-3737. https://doi.org/10.1093/brain/awt269

Almor, A., Kempler, D., MacDonald, M. C., Andersen, E. S., & Tyler, L. K. (1999). Why Do Alzheimer Patients Have Difficulty with Pronouns? Working Memory, Semantics, and Reference in Comprehension and Production in Alzheimer's Disease. *Brain and Language*, *67*(3), 202-227. https://doi.org/10.1006/brln.1999.2055

Aluísio, Sandra Maria, Cunha, A., & Scarton, C. (2016). Evaluating progression of Alzheimer's disease by regression and classification methods in a narrative language test in Portuguese. In Ribeiro, R., Quaresma, P., A. Adami, & A. Branco (Éds.), *Computational Processing of the Portuguese Language* (p. 109-114). Springer International Publishing.

Aminoff, E. M., Kveraga, K., & Bar, M. (2013). The role of the parahippocampal cortex in cognition. *Trends in Cognitive Sciences*, *17*(8), 379-390. https://doi.org/10.1016/j.tics.2013.06.009

Armstrong, E. (2000). Aphasic discourse analysis : The story so far. *Aphasiology*, *14*(9), 875-892. https://doi.org/10.1080/02687030050127685

Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *NeuroImage*, *38*(1), 95-113. https://doi.org/10.1016/j.neuroimage.2007.07.007

Ashburner, J., & Friston, K. J. (2005). Unified segmentation. *NeuroImage*, *26*(3), 839-851. https://doi.org/10.1016/j.neuroimage.2005.02.018

Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate : A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society: Series B (Methodological)*, *57*(1), 289-300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

Bialystok, E. (2021). Bilingualism : Pathway to Cognitive Reserve. *Trends in Cognitive Sciences*, *25*(5), 355-364. https://doi.org/10.1016/j.tics.2021.02.003

Bittner, D., Frankenberg, C., & Schröder, J. (2022). Changes in Pronoun Use a Decade before Clinical Diagnosis of Alzheimer's Dementia—Linguistic Contexts Suggest Problems in Perspective-Taking. *Brain Sciences*, *12*(1), 121. https://doi.org/10.3390/brainsci12010121

Borelli, W. V., Zimmer, E. R., Bieger, A., Coelho, B., Pascoal, T. A., Chaves, M. L. F., Amariglio, R., & Castilhos, R. M. (2022). Subjective cognitive decline in Brazil : Prevalence and association with dementia modifiable risk factors in a population-based study. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *14*(1). https://doi.org/10.1002/dad2.12368

Brandão, L., Lima, T. M., Parente, M. A. de M. P., & Peña-Casanova, J. (2013). Discourse coherence and its relation with cognition in Alzheimer's disease. *Psicologia em Pesquisa*, *7*(1), 99-107. https://dx.doi.org/10.5327/Z1982-1247201300010011

Brucki, S. M. D., Nitrin, R., Caramelli, P., Bertolucci, P. H. F., & Okamoto, I. H. (2003). Sugestões para o uso do mini-exame do estado mental no Brasil. *Arquivos de Neuro-Psiquiatria*, *61*(3 B), 777-781. https://doi.org/10.1590/S0004-282X2003000500014

Bryant, L., Ferguson, A., & Spencer, E. (2016). Linguistic analysis of discourse in aphasia : A review of the literature. *Clinical Linguistics & Phonetics*, *30*(7). https://doi.org/10.3109/02699206.2016.1145740

Bucks, R. S., Singh, S., Cuerden, J. M., & Wilcock, G. K. (2000). Analysis of spontaneous, conversational speech in dementia of Alzheimer type : Evaluation of an objective technique for analysing lexical performance. *Aphasiology*, *14*(1), 71-91. https://doi.org/10.1080/026870300401603

Busatto, G. F., Garrido, G. E. J., Almeida, O. P., Castro, C. C., Camargo, C. H. P., Cid, C. G., Buchpiguel, C. A., Furuie, S., & Bottino, C. M. (2003). A voxel-based morphometry study of temporal lobe gray matter reductions in Alzheimer's disease. *Neurobiology of Aging*, *24*(2), 221-231. https://doi.org/10.1016/S0197-4580(02)00084-2

Caviness, Verne Strudwick, Theodore Lange, N., Makris, N., Reed Herbert, M., & Nelson Kennedy, D. (1999). MRI-based brain volumetrics : Emergence of a developmental brain science. *Brain and Development*, *21*(5), 289-295. https://doi.org/10.1016/S0387-7604(99)00022-4

Chapleau, M., Aldebert, J., Montembeault, M., & Brambati, S. M. (2016). Atrophy in Alzheimer's Disease and Semantic Dementia : An ALE Meta-Analysis of Voxel-Based Morphometry Studies. *Journal of Alzheimer's Disease*, *54*(3), 941-955. https://doi.org/10.3233/JAD-160382

Chen, Y., Lv, C., Li, X., Zhang, J., Chen, K., Liu, Z., Li, H., Fan, J., Qin, T., Luo, L., & Zhang, Z. (2019). The positive impacts of early-life education on cognition, leisure activity, and brain structure in healthy aging. *Aging*, *11*(14), 4923-4942. https://doi.org/10.18632/aging.102088

Cho, S., Cousins, K. A. Q., Shellikeri, S., Ash, S., Irwin, D. J., Liberman, M. Y., Grossman, M., & Nevler, N. (2022). Lexical and Acoustic Speech Features Relating to Alzheimer Disease Pathology. *Neurology*, *99*(4), e313-e322. https://doi.org/10.1212/WNL.0000000000200581

Clark, L. J., Gatz, M., Zheng, L., Chen, Y.-L., McCleary, C., & Mack, W. J. (2009). Longitudinal Verbal Fluency in Normal Aging, Preclinical, and Prevalent Alzheimer's Disease. *American Journal of Alzheimer's Disease & Other Dementiasr*, *24*(6), 461-468. https://doi.org/10.1177/1533317509345154

Clinton, V., Taylor, T., Bajpayee, S., Davison, M. L., Carlson, S. E., & Seipel, B. (2020). Inferential comprehension differences between narrative and expository texts : A systematic review and meta-analysis. *Reading and Writing*, *33*(9), 2223-2248. https://doi.org/10.1007/s11145-020-10044-2

Cotrena, C., Branco, L. D., Cardoso, C. O., Wong, C. E. I., & Fonseca, R. P. (2016). The Predictive Impact of Biological and Sociocultural Factors on Executive Processing : The Role of Age, Education, and Frequency of Reading and Writing Habits. *Applied Neuropsychology: Adult*, *23*(2), 75-84. https://doi.org/10.1080/23279095.2015.1012760

Crosson, B., Benefield, H., Allison Cato, M., Sadek, J. R., Gopinath, K., Soltysik, D., Bauer, R. M., Auerbach, E. J., Gokcay, D., Leonard, C. M., & Briggs, R. W. (2001). Left parahippocampal gyrus activity during language generation. *NeuroImage*, *13*(6), 521. https://doi.org/10.1016/S1053-8119(01)91864-6

Dijkstra, K., Bourgeois, M. S., Allen, R. S., & Burgio, L. D. (2004). Conversational coherence : Discourse analysis of older adults with and without dementia. *Journal of Neurolinguistics*, *17*(4), 263-283. https://doi.org/10.1016/S0911-6044(03)00048-4

Drummond, C., Coutinho, G., Fonseca, R. P., AssunÃ§Ã£o, N., Teldeschi, A., de Oliveira-Souza, R., Moll, J., Tovar-Moll, F., & Mattos, P. (2015). Deficits in narrative discourse elicited by visual stimuli are already present in patients with mild cognitive impairment. *Frontiers in Aging Neuroscience*, *7*. https://doi.org/10.3389/fnagi.2015.00096

Dubois, B., Chupin, M., Hampel, H., Lista, S., Cavedo, E., Croisile, B., Louis Tisserand, G., Touchon, J., Bonafe, A., Ousset, P. J., Ait Ameur, A., Rouaud, O., Ricolfi, F., Vighetto, A., Pasquier, F., Delmaire, C., Ceccaldi, M., Girard, N., Dufouil, C., … "Hippocampus Study Group". (2015). Donepezil decreases annual rate of hippocampal atrophy in suspected prodromal Alzheimer's disease. *Alzheimer's & Dementia*, *11*(9), 1041-1049. https://doi.org/10.1016/j.jalz.2014.10.003

Duong, A., Giroux, F., Tardif, A., & Ska, B. (2005). The heterogeneity of picture-supported narratives in Alzheimer's disease. *Brain and Language*, *93*(2), 173-184. https://doi.org/10.1016/j.bandl.2004.10.007

Duong, A., Tardif, A., & Ska, B. (2003). Discourse about discourse : What is it and how does it progress in Alzheimer's disease? *Brain and Cognition*, *53*(2), 177-180. https://doi.org/10.1016/S0278-2626(03)00104-0

Edmonds, E. C., Delano-Wood, L., Galasko, D. R., Salmon, D. P., & Bondi, M. W. (2015). Subtle Cognitive Decline and Biomarker Staging in Preclinical Alzheimer's Disease. *Journal of Alzheimer's Disease*, *47*(1), 231-242. https://doi.org/10.3233/JAD-150128

Ewers, M., Walsh, C., Trojanowski, J. Q., Shaw, L. M., Petersen, R. C., Jack, C. R., Feldman, H. H., Bokde, A. L. W., Alexander, G. E., Scheltens, P., Vellas, B., Dubois, B., Weiner, M., & Hampel, H. (2012). Prediction of conversion from mild cognitive impairment to Alzheimer's disease dementia based upon biomarkers and neuropsychological test performance. *Neurobiology of Aging*, *33*(7), 1203-1214.e2. https://doi.org/10.1016/j.neurobiolaging.2010.10.019

Filiou, R.-P., Bier, N., Slegers, A., Houzé, B., Belchior, P., & Brambati, S. M. (2020). Connected speech assessment in the early detection of Alzheimer's disease and mild cognitive impairment : A scoping review. *Aphasiology*, *34*(6), 723-755. https://doi.org/10.1080/02687038.2019.1608502

Forbes, K. E., Shanks, M. F., & Venneri, A. (2004). The evolution of dysgraphia in Alzheimer's disease. *Brain Research Bulletin*, *63*(1), 19-24. https://doi.org/10.1016/j.brainresbull.2003.11.005

Forbes-McKay, K. E., & Venneri, A. (2005). Detecting subtle spontaneous language decline in early Alzheimer's disease with a picture description task. *Neurological Sciences*, *26*(4), 243-254. https://doi.org/10.1007/s10072-005-0467-9

Fraser, K. C., Meltzer, J. A., & Rudzicz, F. (2016). Linguistic Features Identify Alzheimer's Disease in Narrative Speech. *Journal of Alzheimer's Disease*, *49*(2), 407-422. https://doi.org/10.3233/JAD-150520

Fratiglioni, L., Viitanen, M., von Strauss, E., Tontodonati, V., Herlitz, A., & Winblad, B. (1997). Very Old Women at Highest Risk of Dementia and Alzheimer's Disease : Incidence Data from the Kungsholmen Project, Stockholm. *Neurology*, *48*(1), 132-138. https://doi.org/10.1212/WNL.48.1.132

Fratiglioni, L., & Wang, H.-X. (2007). Brain Reserve Hypothesis in Dementia. *Journal of Alzheimer's Disease*, *12*(1), 11-22. https://doi.org/10.3233/JAD-2007-12103

Frisoni, G. B. (2002). Detection of grey matter loss in mild Alzheimer's disease with voxel based morphometry. *Journal of Neurology, Neurosurgery & Psychiatry*, *73*(6), 657-664. https://doi.org/10.1136/jnnp.73.6.657

Fyndanis, V., Arfani, D., Varlokosta, S., Burgio, F., Maculan, A., Miceli, G., Arcara, G., Palla, F., Cagnin, A., Papageorgiou, S. G., & Semenza, C. (2018). Morphosyntactic production in Greek- and Italian-speaking individuals with probable Alzheimer's disease : Evidence from subject–verb agreement, tense/time reference, and mood. *Aphasiology*, *32*(1), 61-87. https://doi.org/10.1080/02687038.2017.1358352

García, A. M., De Leon, J., Tee, B. L., Blasi, D. E., & Gorno-Tempini, M. L. (2023). Speech and language markers of neurodegeneration : A call for global equity. *Brain*, awad253. https://doi.org/10.1093/brain/awad253

Graesser, A. C., & McNamara, D. S. (2011). Computational Analyses of Multilevel Discourse Comprehension. *Topics in Cognitive Science*, *3*(2), 371-398. https://doi.org/10.1111/j.1756-8765.2010.01081.x

Graesser, A. C., McNamara, D. S., & Kulikowich, J. M. (2011). Coh-Metrix : Providing Multilevel Analyses of Text Characteristics. *Educational Researcher*, *40*(5), 223-234. https://doi.org/10.3102/0013189X11413260

Graesser, A. C., McNamara, D. S., Louwerse, M. M., & Cai, Z. (2004). Coh-Metrix : Analysis of text on cohesion and language. *Behavior Research Methods, Instruments, & Computers*, *36*(2), 193-202. https://doi.org/10.3758/BF03195564

Hübner, L. C., Loureiro, F. S., Smidarle, A. D., Tessaro, B., Siqueira, E. C. G., Jerônimo, G. M., Quadros, T. D. de, Garcia, V. R. M., & Kochhann, R. (2019). Bateria de Avaliação da Linguagem no Envelhecimento (BALE). In N. Zimmermann, F. J. Delaere, & R. P. Fonseca (Éds.), *Tarefas para Avaliação Neuropsicológica 3 : Avaliação de memória episódica, percepção, linguagem e componentes executivos para adultos* (p. 188-218). Memnon.

Huilt, L. M., Fahey, K. R., & Howard, M. R. (2011). *Born to talk : An introduction to speech and language development*. Pearson Higher Ed.

Jahn, H. (2013). Memory loss in Alzheimer's disease. *Dialogues in Clinical Neuroscience*, *15*(4), 445-454. https://doi.org/10.31887/DCNS.2013.15.4/hjahn

Jarvis, S. (2013). Capturing the Diversity in Lexical Diversity : Lexical Diversity. *Language Learning*, *63*, 87-106. https://doi.org/10.1111/j.1467-9922.2012.00739.x

Jones, B. F., Barnes, J., Uylings, H. B. M., Fox, N. C., Frost, C., Witter, M. P., & Scheltens, P. (2006). Differential Regional Atrophy of the Cingulate Gyrus in Alzheimer Disease : A Volumetric MRI Study. *Cerebral Cortex*, *16*(12), 1701-1708. https://doi.org/10.1093/cercor/bhj105

Kavé, G., & Goral, M. (2016). Word retrieval in picture descriptions produced by individuals with Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology*, *38*(9), 958-966. https://doi.org/10.1080/13803395.2016.1179266

Kavé, G., & Goral, M. (2018). Word retrieval in connected speech in Alzheimer's disease : A review with meta-analyses. *Aphasiology*, *32*(1), 4-26. https://doi.org/10.1080/02687038.2017.1338663

Kavé, G., & Levy, Y. (2003). Morphology in Picture Descriptions Provided by Persons With Alzheimer's Disease. *Journal of Speech, Language, and Hearing Research*, *46*(2), 341-352. https://doi.org/10.1044/1092-4388(2003/027)

Kim, R. E., Lee, M., Kang, D. W., Wang, S.-M., Kim, D., & Lim, H. K. (2023). Effects of education mediated by brain size on regional brain volume in adults. *Psychiatry Research: Neuroimaging*, *330*, 111600. https://doi.org/10.1016/j.pscychresns.2023.111600

Kong, A. P.-H., Whiteside, J., & Bargmann, P. (2016). The Main Concept Analysis : Validation and sensitivity in differentiating discourse produced by unimpaired English speakers from individuals with aphasia and dementia of Alzheimer type. *Logopedics Phoniatrics Vocology*, *41*(3), 129-141. https://doi.org/10.3109/14015439.2015.1041551

Labache, L., Joliot, M., Saracco, J., Jobard, G., Hesling, I., Zago, L., Mellet, E., Petit, L., Crivello, F., Mazoyer, B., & Tzourio-Mazoyer, N. (2019). A SENtence Supramodal Areas AtlaS (SENSAAS) based on multiple task-induced activation mapping and graph analysis of intrinsic connectivity in 144 healthy right-handers. *Brain Structure and Function*, *224*(2), 859-882. https://doi.org/10.1007/s00429-018-1810-2

Leal, S. E., Duran, M. S., Scarton, C. E., Hartmann, N. S., & Aluísio, S. M. (2022). *NILC-Metrix : Assessing the complexity of written and spoken language in Brazilian Portuguese*. https://doi.org/10.48550/ARXIV.2201.03445

Leube, D. T., Weis, S., Freymann, K., Erb, M., Jessen, F., Heun, R., Grodd, W., & Kircher, T. T. (2008). Neural correlates of verbal episodic memory in patients with MCI and Alzheimer's disease—A VBM study. *International Journal of Geriatric Psychiatry*, *23*(11), 1114-1118. https://doi.org/10.1002/gps.2036

Lindsay, H., Tröger, J., & König, A. (2021). Language Impairment in Alzheimer's Disease—Robust and Explainable Evidence for AD-Related Deterioration of Spontaneous Speech Through Multilingual Machine Learning. *Frontiers in Aging Neuroscience*, *13*, 642033. https://doi.org/10.3389/fnagi.2021.642033

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns, A., Cohen-Mansfield, J., Cooper, C., Costafreda, S. G., Dias, A., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M., Larson, E. B., Ogunniyi, A., … Mukadam, N. (2020). Dementia prevention, intervention, and care : 2020 report of the Lancet Commission. *The Lancet*, *396*(10248), 413-446. https://doi.org/10.1016/S0140-6736(20)30367-6

Lorca-Puls, D. L., Gajardo-Vidal, A., White, J., Seghier, M. L., Leff, A. P., Green, D. W., Crinion, J. T., Ludersdorfer, P., Hope, T. M. H., Bowman, H., & Price, C. J. (2018). The impact of sample size on the reproducibility of voxel-based lesion-deficit mappings. *Neuropsychologia*, *115*, 101-111. https://doi.org/10.1016/j.neuropsychologia.2018.03.014

Lukic, S., Thompson, C. K., Barbieri, E., Chiappetta, B., Bonakdarpour, B., Kiran, S., Rapp, B., Parrish, T. B., & Caplan, D. (2021). Common and distinct neural substrates of sentence production and comprehension. *NeuroImage*, *224*. https://doi.org/10.1016/j.neuroimage.2020.117374

Luzzi, S., Baldinelli, S., Ranaldi, V., Fiori, C., Plutino, A., Fringuelli, F. M., Silvestrini, M., Baggio, G., & Reverberi, C. (2020). The neural bases of discourse semantic and pragmatic deficits in patients with frontotemporal dementia and Alzheimer's disease. *Cortex*, *128*, 174-191. https://doi.org/10.1016/j.cortex.2020.03.012

Mackenzie, C. (2000). The relevance of education and age in the assessment of discourse comprehension. *Clinical Linguistics & Phonetics*, *14*(2), 151-161. https://doi.org/10.1080/026992000298887

Manjón, J. V., Coupé, P., Martí-Bonmatí, L., Collins, D. L., & Robles, M. (2010). Adaptive non-local means denoising of MR images with spatially varying noise levels : Spatially Adaptive Nonlocal Denoising. *Journal of Magnetic Resonance Imaging*, *31*(1), 192-203. https://doi.org/10.1002/jmri.22003

Manly, J. J., Schupf, N., Tang, M.-X., & Stern, Y. (2005). Cognitive Decline and Literacy Among Ethnically Diverse Elders. *Journal of Geriatric Psychiatry and Neurology*, *18*(4), 213-217. https://doi.org/10.1177/0891988705281868

Mar, R. A., Li, J., Nguyen, A. T. P., & Ta, C. P. (2021). Memory and comprehension of narrative versus expository texts : A meta-analysis. *Psychonomic Bulletin & Review*, *28*(3), 732-749. https://doi.org/10.3758/s13423-020-01853-1

Marini, A., Andreetta, S., del Tin, S., & Carlomagno, S. (2011). A multi-level approach to the analysis of narrative language in aphasia. *Aphasiology*, *25*(11), 1372-1392. https://doi.org/10.1080/02687038.2011.584690

Martin, C.-O., Desrochers, M., Demers, C., Scherer, L. C., & Ska, B. (2012). Influence of reading habits on cerebral plasticity for discourse comprehension in aging. *Ilha do Desterro A Journal of English Language, Literatures in English and Cultural Studies*, *0*(63). https://doi.org/10.5007/2175-8026.2012n63p101

Martin, C.-O., Pontbriand-Drolet, S., Daoust, V., Yamga, E., Amiri, M., Hübner, L. C., & Ska, B. (2018). Narrative Discourse in Young and Older Adults : Behavioral and NIRS Analyses. *Frontiers in Aging Neuroscience*, *10*. https://doi.org/10.3389/fnagi.2018.00069

Mascali, D., DiNuzzo, M., Serra, L., Mangia, S., Maraviglia, B., Bozzali, M., & Giove, F. (2018). Disruption of Semantic Network in Mild Alzheimer's Disease Revealed by Resting-State fMRI. *Neuroscience*, *371*, 38-48. https://doi.org/10.1016/j.neuroscience.2017.11.030

Mehler, J. (1994). Cross-linguistic approaches to speech processing. *Current Opinion in Neurobiology*, *4*(2), 171-176. https://doi.org/10.1016/0959-4388(94)90068-X

Mellard, D. F., Fall, E., & Woods, K. L. (2010). A Path Analysis of Reading Comprehension for Adults With Low Literacy. *Journal of Learning Disabilities*, *43*(2), 154-165. https://doi.org/10.1177/0022219409359345

Morris, J. C. (1993). The Clinical Dementia Rating (CDR) : Current version and scoring rules. *Neurology*, *43*(11), 2412.2-2412-a. https://doi.org/10.1212/WNL.43.11.2412-a

Mueller, K. D., Hermann, B., Mecollari, J., & Turkstra, L. S. (2018). Connected speech and language in mild cognitive impairment and Alzheimer's disease : A review of picture description tasks. *Journal of Clinical and Experimental Neuropsychology*, *40*(9), 917-939. https://doi.org/10.1080/13803395.2018.1446513

Nicholas, M., Obler, L. K., Albert, M. L., & Helm-Estabrooks, N. (1985). Empty Speech in Alzheimer's Disease and Fluent Aphasia. *Journal of Speech, Language, and Hearing Research*, *28*(3), 405-410. https://doi.org/10.1044/jshr.2803.405

Oldfield, R. C. (1971). The assessment and analysis of handedness : The Edinburgh inventory. *Neuropsychologia*, *9*(1), 97-113. https://doi.org/10.1016/0028-3932(71)90067-4

PAHO. (2022). *Pan American Health Organization/World Health Organization. Core Indicators Portal*.

Pawlowski, J., Remor, E., de Mattos Pimenta Parente, M. A., de Salles, J. F., Fonseca, R. P., & Bandeira, D. R. (2012). The influence of reading and writing habits associated with education on the neuropsychological performance of Brazilian adults. *Reading and Writing*, *25*(9). https://doi.org/10.1007/s11145-012-9357-8

Pekkala, S., Wiener, D., Himali, J. J., Beiser, A. S., Obler, L. K., Liu, Y., McKee, A., Auerbach, S., Seshadri, S., Wolf, P. A., & Au, R. (2013). Lexical retrieval in discourse : An early indicator of Alzheimer's dementia. *Clinical Linguistics & Phonetics*, *27*(12), 905-921. https://doi.org/10.3109/02699206.2013.815278

Peng, F., Wang, L., Geng, Z., Zhu, Q., & Song, Z. (2016). A Cross-Sectional Voxel-Based Morphometric Study of Age- and Sex-Related Changes in Gray Matter Volume in the Normal Aging Brain: *Journal of Computer Assisted Tomography*, *40*(2), 307-315. https://doi.org/10.1097/RCT.0000000000000351

Petti, U., Baker, S., & Korhonen, A. (2020). A systematic literature review of automatic Alzheimer's disease detection from speech and language. *Journal of the American Medical Informatics Association*, *27*(11), 1784-1797. https://doi.org/10.1093/jamia/ocaa174

Pistono, A., Pariente, J., Bézy, C., Lemesle, B., Le Men, J., & Jucla, M. (2019). What happens when nothing happens? An investigation of pauses as a compensatory mechanism in early Alzheimer's disease. *Neuropsychologia*, *124*, 133-143. https://doi.org/10.1016/j.neuropsychologia.2018.12.018

Pistono, A., Senoussi, M., Guerrier, L., Rafiq, M., Giméno, M., Péran, P., Jucla, M., & Pariente, J. (2021). Language Network Connectivity Increases in Early Alzheimer's Disease. *Journal of Alzheimer's Disease*, *82*(1), 447-460. https://doi.org/10.3233/JAD-201584

Prince, M., Bryce, R., Albanese, E., Wimo, A., Ribeiro, W., & Ferri, C. P. (2013). The global prevalence of dementia : A systematic review and metaanalysis. *Alzheimer's & Dementia*, *9*(1), 63. https://doi.org/10.1016/j.jalz.2012.11.007

Prins, R., & Bastiaanse, R. (2004). Review. *Aphasiology*, *18*(12), 1075-1091. https://doi.org/10.1080/02687030444000534

Richards, M., & Sacker, A. (2003). Lifetime Antecedents of Cognitive Reserve. *Journal of Clinical and Experimental Neuropsychology*, *25*(5), 614-624. https://doi.org/10.1076/jcen.25.5.614.14581

Rorden, C., & Brett, M. (2000). Stereotaxic Display of Brain Lesions. *Behavioural Neurology*, *12*(4), 191-200. https://doi.org/10.1155/2000/421719

Roumpea, G., Nousia, A., Stavrakaki, S., Nasios, G., & Manouilidou, C. (2019). Lexical and grammatical aspect in Mild Cognitive Impairment and Alzheimer's disease. *Selected Papers on Theoretical and Applied Linguistics*, *Vol 23*, 381-397 Pages. https://doi.org/10.26262/ISTAL.V23I0.7355

Sangha, O., Ma, D., Popuri, K., Stocks, J., Wang, L., & Beg, M. F. (2021). Structural volume and cortical thickness differences between males and females in cognitively normal, cognitively impaired and Alzheimer's dementia population. *Neurobiology of Aging*, *106*, 1-11. https://doi.org/10.1016/j.neurobiolaging.2021.05.018

Scheff, S. W., Price, D. A., Schmitt, F. A., Scheff, M. A., & Mufson, E. J. (2011). Synaptic Loss in the

Inferior Temporal Gyrus in Mild Cognitive Impairment and Alzheimer's Disease. *Journal of Alzheimer's Disease*, *24*(3), 547-557. https://doi.org/10.3233/JAD-2011-101782

Schneider, F., Marcotte, K., Brisebois, A., Townsend, S. A. M., Smidarle, A. D., Loureiro, F., da Rosa Franco, A., Soder, R. B., Nikolaev, A., Marrone, L. C. P., & Hübner, L. C. (2021). Neuroanatomical Correlates of Macrolinguistic Aspects in Narrative Discourse in Unilateral Left and Right Hemisphere Stroke : A Voxel-Based Morphometry Study. *Journal of Speech, Language, and Hearing Research*. https://doi.org/10.1044/2020_JSLHR-20-00500

Schneider, F., Marcotte, K., Brisebois, A., Townsend, S. A. M., Smidarle, A. D., Soder, R. B., Marrone, L. C. P., & Hübner, L. C. (2022). Macrostructural aspects in oral narratives in Brazilian Portuguese by left and right hemisphere stroke patients with low education and low socioeconomic status. *American Journal of Speech-Language Pathology*, *31*(3), 1319-1337. https://doi.org/10.1044/2021_AJSLP-21-00205

Shapiro, A. M. (2004). How Including Prior Knowledge As a Subject Variable May Change Outcomes of Learning Research. *American Educational Research Journal*, *41*(1), 159-189. https://doi.org/10.3102/00028312041001159

Ska, B., Duong, A., & Joanette, Y. (2004). Discourse impairments. In R. D. Kent (Éd.), *The MIT encyclopedia of communication disorders* (p. 302-304). The MIT press.

Slegers, A., Filiou, R.-P., Montembeault, M., & Brambati, S. M. (2018). Connected Speech Features from Picture Description in Alzheimer's Disease : A Systematic Review. *Journal of Alzheimer's Disease*, *65*(2). https://doi.org/10.3233/JAD-170881

Smith, S. M., Zhang, Y., Jenkinson, M., Chen, J., Matthews, P. M., Federico, A., & De Stefano, N. (2002). Accurate, Robust, and Automated Longitudinal and Cross-Sectional Brain Change Analysis. *NeuroImage*, *17*(1), 479-489. https://doi.org/10.1006/nimg.2002.1040

Song, T., Pan, Y., Chen, R., Li, H., Zhao, X., Liu, L., Wang, C., Wang, Y., & Wang, Y. (2017). Is there a correlation between socioeconomic disparity and functional outcome after acute ischemic stroke? *PLoS ONE*. https://doi.org/10.1371/journal.pone.0181196

Stark, B. C., Bryant, L., Themistocleous, C., den Ouden, D.-B., & Roberts, A. C. (2022). Best practice guidelines for reporting spoken discourse in aphasia and neurogenic communication disorders. *Aphasiology*, 1-24. https://doi.org/10.1080/02687038.2022.2039372

Stark, B. C., Dutta, M., Murray, L. L., Bryant, L., Fromm, D., MacWhinney, B., Ramage, A. E., Roberts, A., den Ouden, D. B., Brock, K., McKinney-Bock, K., Paek, E. J., Harmon, T. G., Yoon, S. O., Themistocleous, C., Yoo, H., Aveni, K., Gutierrez, S., & Sharma, S. (2021). Standardizing Assessment of Spoken Discourse in Aphasia : A Working Group With Deliverables. *American Journal of Speech-Language Pathology*, *30*(1S). https://doi.org/10.1044/2020_AJSLP-19-00093

Stern, Y. (2009). Cognitive reserve☆. *Neuropsychologia*, *47*(10), 2015-2028. https://doi.org/10.1016/j.neuropsychologia.2009.03.004

Stern, Y., Alexander, G. E., Prohovnik, I., Stricks, L., Link, B., Lennon, M. C., & Mayeux, R. (1995). Relationship between lifetime occupation and parietal flow : Implications for a reserve against Alzheimer's disease pathology. *Neurology*, *45*(1), 55-60. https://doi.org/10.1212/WNL.45.1.55

Szatloczki, G., Hoffmann, I., Vincze, V., Kalman, J., & Pakaski, M. (2015). Speaking in Alzheimer's Disease, is That an Early Sign? Importance of Changes in Language Abilities in Alzheimer's Disease. *Frontiers in Aging Neuroscience*, *7*. https://doi.org/10.3389/fnagi.2015.00195

Taler, V., & Phillips, N. A. (2008). Language performance in Alzheimer's disease and mild cognitive impairment : A comparative review. *Journal of Clinical and Experimental Neuropsychology*, *30*(5), 501-556. https://doi.org/10.1080/13803390701550128

Thompson, C. K., Cho, S., Hsu, C.-J., Wieneke, C., Rademaker, A., Weitner, B. B., Mesulam, M. M., &

Weintraub, S. (2012). Dissociations between fluency and agrammatism in primary progressive aphasia. *Aphasiology*, *26*(1), 20-43. https://doi.org/10.1080/02687038.2011.584691

Toledo, C. M., Aluísio, S. M., Santos, L. B., Brucki, S. M. D., Trés, E. S., Oliveira, M. O., & Mansur, L. L. (2018). Analysis of macrolinguistic aspects of narratives from individuals with Alzheimer's disease, mild cognitive impairment, and no cognitive impairment. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *10*(1), 31-40. https://doi.org/10.1016/j.dadm.2017.08.005

United Nations, Department of Economic and Social Affairs, Population Division. (2019). *World Population Ageing 2019 : Highlights*.

United Nations Development Programme. (2020). *Education Index*. Human Development Reports.

Uysal, G., & Ozturk, M. (2020). Hippocampal atrophy based Alzheimer's disease diagnosis via machine learning methods. *Journal of Neuroscience Methods*, *337*, 108669. https://doi.org/10.1016/j.jneumeth.2020.108669

Walhovd, K. B., Fjell, A. M., Wang, Y., Amlien, I. K., Mowinckel, A. M., Lindenberger, U., Düzel, S., Bartrés-Faz, D., Ebmeier, K. P., Drevon, C. A., Baaré, W. F. C., Ghisletta, P., Johansen, L. B., Kievit, R. A., Henson, R. N., Madsen, K. S., Nyberg, L., R Harris, J., Solé-Padullés, C., … Brandmaier, A. M. (2022). Education and Income Show Heterogeneous Relationships to Lifespan Brain and Cognitive Differences Across European and US Cohorts. *Cerebral Cortex*, *32*(4), 839-854. https://doi.org/10.1093/cercor/bhab248

Walhovd, K. B., Lövden, M., & Fjell, A. M. (2023). Timing of lifespan influences on brain and cognition. *Trends in Cognitive Sciences*, *27*(10), 901-915. https://doi.org/10.1016/j.tics.2023.07.001

Wang, W.-Y., Yu, J.-T., Liu, Y., Yin, R.-H., Wang, H.-F., Wang, J., Tan, L., Radua, J., & Tan, L. (2015). Voxel-based meta-analysis of grey matter changes in Alzheimer's disease. *Translational Neurodegeneration*, *4*(1), 6. https://doi.org/10.1186/s40035-015-0027-z

Wechsler, D. (1997). *Wechsler Adult Intelligence Scale* (3rd edition). The Psychological Corporation.

Williams, E., McAuliffe, M., & Theys, C. (2021). Language changes in Alzheimer's disease : A systematic review of verb processing. *Brain and Language*, *223*, 105041. https://doi.org/10.1016/j.bandl.2021.105041

Yogarajah, M., Powell, H. W. R., Parker, G. J. M., Alexander, D. C., Thompson, P. J., Symms, M. R., Boulby, P., Wheeler-Kingshott, C. A., Barker, G. J., Koepp, M. J., & Duncan, J. S. (2008). Tractography of the parahippocampal gyrus and material specific memory impairment in unilateral temporal lobe epilepsy. *NeuroImage*, *40*(4), 1755-1764. https://doi.org/10.1016/j.neuroimage.2007.12.046

Zhu, A. Y. F., Yu, C. W. M., & Chou, K. L. (2021). Improving Financial Literacy in Secondary School Students : An Randomized Experiment. *Youth & Society*, *53*(4), 539-562. https://doi.org/10.1177/0044118X19851311

Table 1. Mean sociodemographic and clinical descriptive data for people with Alzheimer's disease, and age-matched healthy participants.

	Group						Statistics	
	AD (n=9)			WWBI (n=10)				
Variable	**M**	**SD**	**range**	**M**	**SD**	**range**	**t or U**	**p**
Demographic information								
Age	76.22	5.58	68 – 84	72.1	5.7	63 – 82	1.59	.131
Socioeconomic status (SES)	21	7.21	13 – 32	20.4	5.56	13 – 31	.194	.849
Education (years)	6.44	2.45	4 – 11	4.8	2.15	1 – 8	1.56	.138
Reading Habits	4.75	3.73	0 –10	6.5	3.86	0 – 14	-.969	.347
Writing habits	1.38	1.77	0 – 4	5.3	4.37	0 – 12	-2.376	**.030**
Cognitive screening								
Mini-Mental State Examination (/30)	20.67	2.34	17 – 25	27.3	2.49	23 – 30	-5.950	**<.001**
Cognitive testing								
Trail Making Test 1 (sec.)	167.88	96.79	30 – 304	72.20	19.44	49 – 116	3.072	**.007**
Trail Making Test 2 (sec.)	301.17	150.33	90 – 507	156.60	31.71	98 – 217	2.999	**.010**
Episodic Memory Free Total	8.56	7.11	0 – 22	31.3	6.27	22 – 41	-7.412	**<.001**
Episodic Memory Cued Total	16.00	10.36	0 – 31	15.80	5.85	7 – 26	.053	.959
Digit Span Forward	6.89	2.75	4 – 11	6.40	1.17	4 – 8	-4.712	.615
Digit Span Backward	3.33	1.44	0 – 8	3.10	1.45	1 – 5	.264	.795
Language Testing								
Semantic Verbal Fluency	7.56	2.79	3 – 12	15.25	3.37	9 – 19	-5.15	**<.001**
Phonemic Verbal Fluency	6.44	3.47	4 – 14	10.86	4.25	5 – 17	-2.29	**.038**
Semantic Knowledge	3.22	2.28	0 – 7	5.70	3.27	0 – 9	-1.895	.075
Semantic Association	17.44	4.64	12 – 23	22.00	2.11	17 – 24	70.00§	**.043**
Naming	44.00	8.19	30 – 57	55.00	2.67	51 – 59	-4.030	**.001**

Legend:

§ non-parametric test

Note: WWBI = women without brain injury; AD = Alzheimer's disease group; M = mean; SD = Standard deviation; SES = socioeconomic status as calculated by a questionnaire developed by *Associação Brasileira de Empresas de Pesquisa* in 2015: Class A = 45 - 100 points, B1 = 38 – 44 points, B2 = 29 - 37 points, C1 = 23 - 28 points, C2 = 17 - 22 points, D-E = 0 – 16 points).

Table 2. Stereotactic locations of the multiple regressions with the microlinguistic measures of discourse.

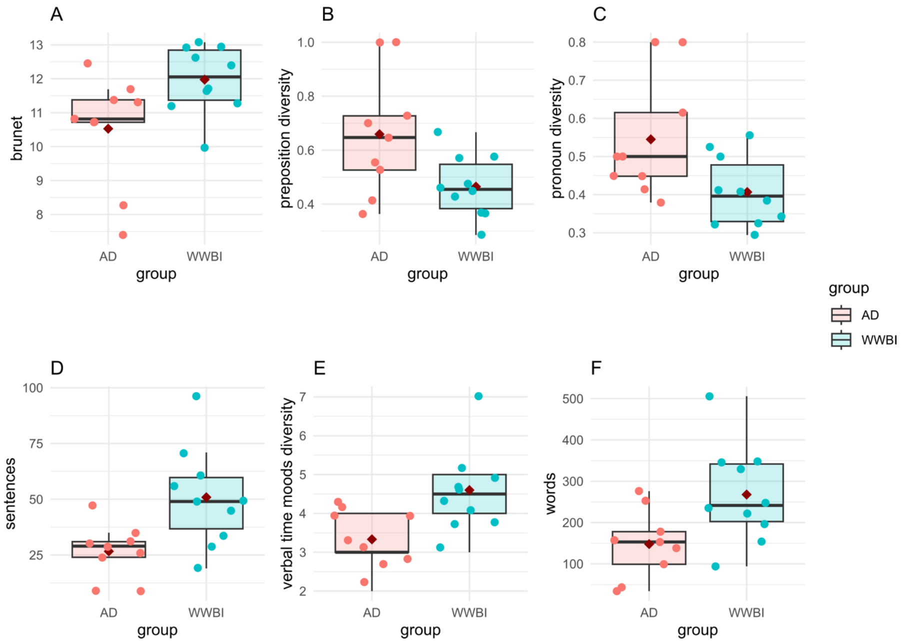
			MNI 152 coordinates						
Microlinguistic variables	**Area**	**Cluster size (k)**	**x**	**y**	**z**	**T**	**df**	**FWE**	**Effect size**
words	Parahippocampal gyrus	842	-24	-20	-33	5.39	16	0.000	0.8030
sentences	Parahippocampal gyrus	441	-24	-20	-33	6.11	16	0.007	0.8366
verbal time mood diversity	Left pallidum, left amygdala	382	-18	-4	-9	4.2	16	0.015	0.7241
	Anterior cingulate gyrus	313	3	46	3	4.58	16	0.038	0.75318

Legend:

df = degrees of freedom

Note: Summary of regions where GM volume was significantly associated with performance in each discourse measures. A family-wise error (FWE) correction at $p < 0.05$ at the cluster level was applied, using an arbitrary cluster-forming uncorrected threshold of $p < 0.001$. Significant peak regions are reported with corresponding MNI coordinates, T and p values, degrees of freedom, and effect sizes ($\sqrt[2]{t^2/(t^2+df)}$).

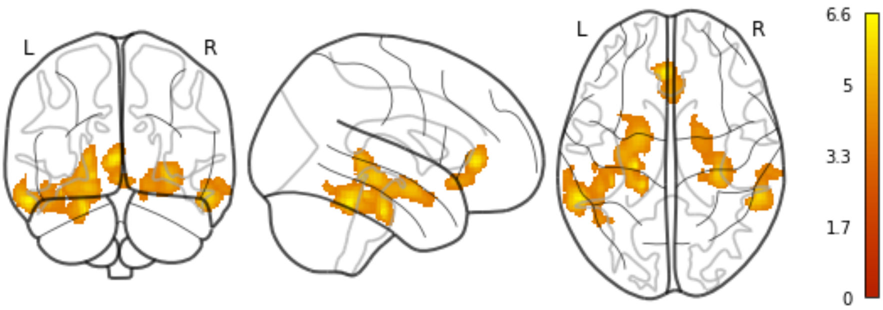
Figure 1. Boxplots comparing AD and WWBI groups in the six variables which showed significant differences between the two groups ($p < 0.05$).



Legend:

Note: A = Brunet's index; B = proposition diversity; C = pronoun diversity; D = number of sentences; E = verbal time mood diversity; F = number of words. The red marks on the boxplots represent the average of the values.

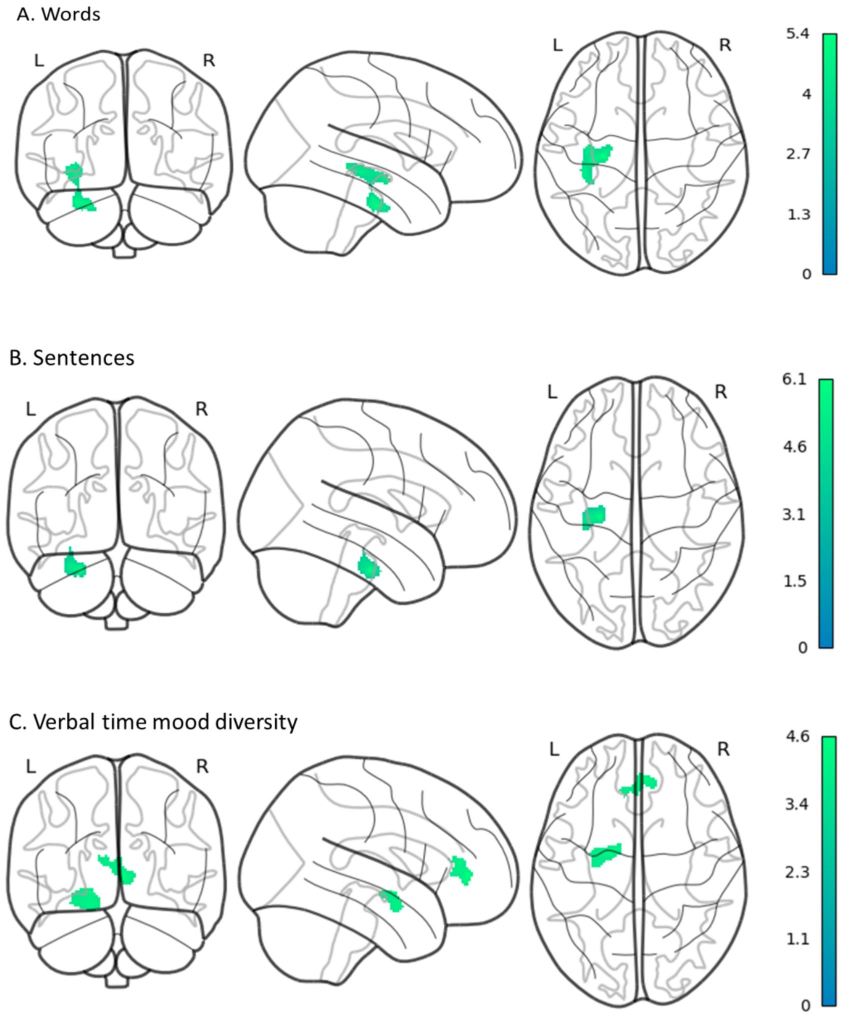
Figure 2. Glass brain rendering showing regions of grey matter loss in the group of women with Alzheimer's disease compared to the group of women without neurological damage.



Legend:

Note: All voxels shown in color survived a family-wise error correction ($p < 0.05$) at the cluster level, using an arbitrary cluster-forming uncorrected threshold ($p < 0.001$). The color bar reflects the range of values from minimum (red) to maximum (yellow).

Figure 3. Glass brain rendering showing regions of grey matter associated with words, sentences, and verbal time mood diversity.

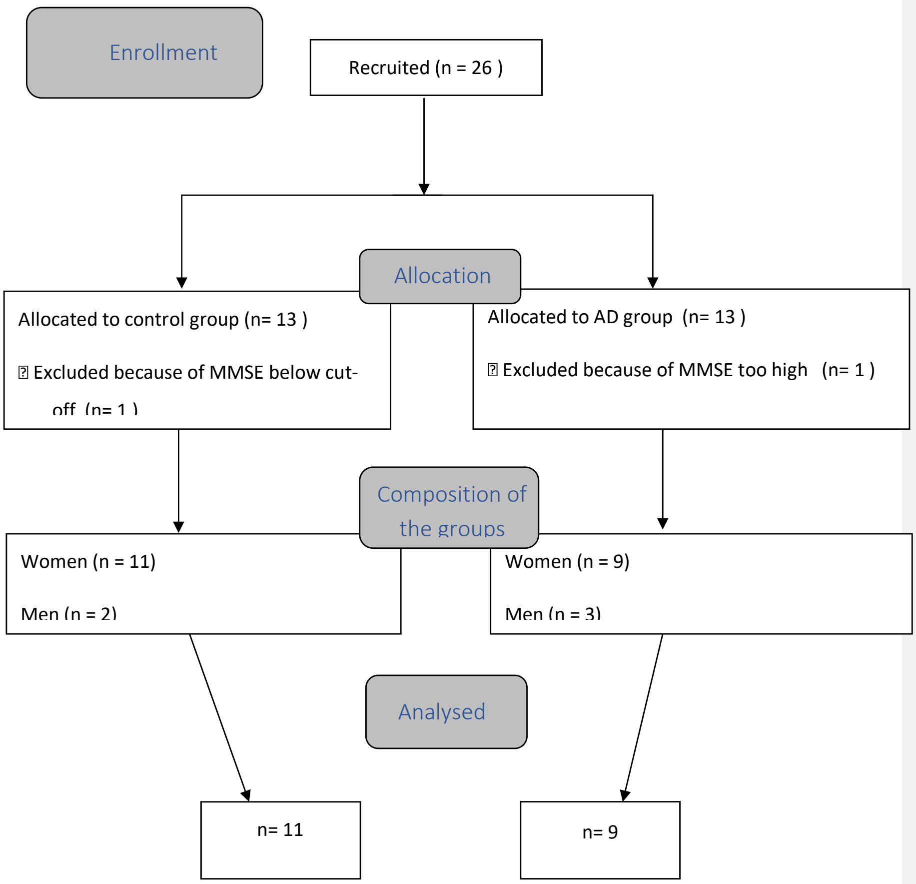


Legend:

Note: All voxels shown in color survived a family-wise error correction ($p < 0.05$) at the cluster level, using an arbitrary cluster-forming uncorrected threshold ($p < 0.001$). The color bar reflects the range of values from minimum (blue) to maximum (green).

Supplementary Material 1. A flow diagram of the progress through the phases of the study (that is, enrolment, group allocation, and data analysis) is reported in Supplementary Material 1.

Supplementary Material 1. Flow diagram of the study recruitment.



Supplementary Table 2. Mean descriptive data and statistical results of the microlinguistic variables extracted from discourse samples distinguishing the AD and the WWBI groups.

		AD (N=9)		WWBI (n=10)			
Linguistic variable	**Category**	**Mean (SD)**	**Minimum-maximum**	**Mean (SD)**	**Minimum-Maximum**	**T-test (*p* value)**	**Corrected *p* value***
Connector ratio	Connector measures	0.09 (0.04)	(0.023, 0.15)	0.12 (0.02)	(0.08, 0.14)	-1.31 (0.20)	0.09
Sentences	Descriptive measures	26.66 (11.99)	(9, 47)	50.9 (22.09)	(19, 96)	-2.92 (0.01)	**0.013**
Words per sentence	Descriptive measures	5.29 (1.24)	(3.77, 7.88)	5.25 (0.43)	(4.79, 6.17)	0.092 (0.92)	0.19
Words	Descriptive measures	147.88 (82.86)	(34, 276)	267.80 (117.81)	(94, 506)	-2.54 (0.02)	**0.02**
Preposition diversity	Lexical diversity	0.66 (0.22)	(0.36, 1)	0.464 (0.11)	(0.28, 0.66)	2.4 (0.02)	**0.02**
Pronoun diversity	Lexical diversity	0.54 (0.16)	(0.38, 0.8)	0.41 (0.09)	(0.29, 0.55)	2.35 (0.03)	**0.04**
Relative clauses	Lexical diversity	0.09 (0.05)	(0, 0.15)	0.06 (0.04)	(0.01, 0.12)	1.96 (0.06)	0.05
Indicative present ratio	Lexical diversity	0.47 (0.2)	(0.11, 0.9)	0.30 (0.16)	(0.06, 0.50)	1.81 (0.08)	0.05
Noun diversity	Lexical diversity	0.73 (0.179)	(0.43, 1)	0.65 (0.07)	(0.56, 0.76)	1.35 (0.19)	0.08
Type-to-token ratio (TTR)	Lexical diversity	0.68 (0.12)	(0.48, 0.91)	0.63 (0.04)	(0.58, 0.70)	1.25 (0.22)	0.09
Content density	Lexical diversity	1.37 (0.30)	(0.94, 1.83)	1.27 (0.16)	(0.92, 1.46)	0.93 (0.38)	0.13
Function-to-content words ratio	Lexical diversity	0.76 (0.17)	(0.54, 1.06)	0.80 (0.12)	(0.68, 1.08)	-0.58 (0.56)	0.15
Content word diversity	Lexical diversity	0.74 (0.10)	(0.58, 0.90)	0.72 (0.053)	(0.64, 0.79)	0.49 (0.62)	0.15
Concreteness mean	Psycholinguistic measures	4.38 (0.34)	(3.8, 4.69	4.57 (0.18)	(4.32, 4.85)	-1.50 (0.15)	0.07
Imageability mean	Psycholinguistic measures	4.74 (0.26)	(4.29, 4.98)	4.86 (0.12)	(4.71, 5.04)	-1.22 (0.27)	0.10
Acquisition age mean	Psycholinguistic measures	2.92 (0.24)	(2.53, 3.35)	2.90 (0.16)	(2.62, 3.08)	0.21(0.84)	0.17
Familiarity mean	Psycholinguistic measures	5.31 (0.069)	(5.10, 5.41)	5.31 (0.08)	(5.17, 5.47)	0.18 (0.85)	0.18
Brunet	Readability measures	10.53 (1.64)	(7.39, 12.45)	11.97 (0.99)	(9.96, 13.07)	-2.35(0.03)	**0.03**
Honore	Readability measures	876.65 (579.63)	(416.48, 2373.79)	721.06 (89.96)	(630.35, 941.03)	0.84(0.41)	0.13

Flesch	Readability measures	90.66 (6.73)	(82.91, 101.59)	90.02 (4.97)	(83.36, 97.56)	0.24(0.81)	0.17
Frazier	Syntax complexity	6.24 (0.40)	(5.38, 6.72)	6.39 (0.27)	(5.96, 7)	-0.95(0.35)	0.12
Yngve	Syntax complexity	1.59 (0.14)	(1.35, 1.83)	1.57 (0.05)	(1.49, 1.68)	0.28(0.78)	0.16
Verbal time mood diversity	Temporal lexicon	3.33 (0.71)	(2, 4)	4.6 (1.07)	(3, 7)	-2.99 (0.01)	**0.006**
Content word frequency	Word frequency	627251.22 (334455.33)	(259314.09, 1235414.37)	519957.64 (152240.29)	(204637.46, 742153.80)	0.92 (0.37)	0.12
Verbs	Word morphosyntactic information	0.26 (0.03)	(0.22, 0.31)	0.23 (0.02)	(0.20, 0.27)	1.77(0.11)	0.06
Noun ratio	Word morphosyntactic information	0.17 (0.04)	(0.11, 0.2)	0.19 (0.02)	(0.17, 0.22)	-1.62 (0.14)	0.06
Inflected verbs	Word morphosyntactic information	0.81 (0.06)	(0.74, 0.91)	0.78 (0.05)	(0.71, 0.88)	1.11(0.28)	0.11
Pronoun ratio	Word morphosyntactic information	0.165 (0.04)	(0.08, 0.23)	0.15 (0.03)	(0.09, 0.20)	0.83 (0.42)	0.14
Infinitive verbs	Word morphosyntactic information	0.107 (0.04)	(0.05, 0.2)	0.10 (0.04)	(0.03, 0.15)	0.07 (0.94)	0.20

*corrected *p* value using the Benjamini-Hochberg procedure.
AD = Alzheimer's disease group; WWBI = women without brain injury; M = mean; SD = Standard deviation.