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Discriminating speech traits of Alzheimer's disease assessed through a corpus of reading task for Spanish language

Olga Ivanova [a,c,*], Juan José G. Meilán [b,c], Francisco Martínez-Sánchez [d], Israel Martínez-Nicolás [b,c], Thide E. Llorente [b,c], Nuria Carcavilla González [c,e]

[a] Faculty of Philology, University of Salamanca, Spain, Plaza de Anaya s/n, Salamanca, 37008 Spain
[b] Faculty of Psychology, University of Salamanca, Spain, Avenida de la Merced 109, Salamanca, 37005 Spain
[c] Institute of Neurosciences of Castilla y León, Spain, Pintor Fernando Gallego 1, Salamanca, 37007 Spain
[d] Faculty of Psychology, University of Murcia, Spain, Campus de Espinardo, Building 31, Murcia, 30100 Spain
[e] Faculty of Health Sciences, Public University of Navarre, Spain, Campus Arrosadia, Building Los Magnolios, Pamplona, 31006 Spain

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ABSTRACT

It is estimated that between 50% and 75% of all cases of dementia are due to Alzheimer's disease (AD), the most common neurodegenerative disease among World population. However, a long preclinical period of AD makes it difficult to differentiate between people with Mild Cognitive Impairment (MCI) that would progress to dementia from people with MCI that would not. One of the most promising solutions to detect MCI which will evolve to dementia (preAD) comes from the field of automatic speech analysis. Speech is a complex physiological and neurocognitive language-mediated process, which can be significantly altered in pathological aging and exhibit high levels of sensitivity for the diagnosis of neurological diseases. The purpose of this research is to offer a detailed perspective on the speech changes in MCI and mild AD when compared to healthy aging (HA), that would allow to detect pathological processes prior to the clinical expression of AD. Based on our previous research record on speech in HA, MCI and AD, we provide a global review of dementia-related speech traits and propose a reading-based protocol for assessing ongoing neurodegenerative processes in the elderly. We report the results of speech analysis in elderly people with different cognitive profiles, who performed a standardized reading task and were further analyzed for correlations between neurocognitive assessment indicative of cognitive impairment stage (HA, MCI or AD) and acoustic, temporal and prosodic traits in speech. We show that evolution from HA to AD exhibits a steady pattern of speech changes in parallel to the cognitive decline, which consists in significant increase in duration and phonation time, extension of pauses and voice breaks, intensification of variation in syllabic production, and decrease in speech energy and intensity leading to dysphony. In doing so, we prove that a standardized reading task is a very useful type of stimuli for detecting dementia-related speech traits and, in view of this, we discuss the relevance of reading for preclinical automated diagnosis of AD. The main contribution of this paper is a corpus of recordings of the standardized reading task performed by healthy elderly people and people with MCI and AD in Spanish language, and which can be used for further research purposes. In this respect, our work fills an important gap existing in corpora-based studies of speech and language impairments related to progression to dementia.

; AD, Alzheimer's disease; MCI, Mild Cognitive Impairment.

* Corresponding author
E-mail address: olga.ivanova@usal.es (O. Ivanova).

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1. Introduction

1.1. Early discrimination of Alzheimer's disease

Scholars systematically point out the necessity to improve cognitive screening tools for the early detection of dementia-related Mild Cognitive Impairment (MCI). In this regard, there are highly reliable biomarkers, like protein concentration in cerebrospinal fluid (CSF) (Blennow and Zetterberg 2018; Lim et al., 2019), and other important general tests like brain imaging or blood samples (Robinson et al., 2017). However, cognitive screening is frequently faster and easier to apply, less invasive for the patient and, importantly, rather less subject to long delays in clinical attendance, and do not represent significant economic burden for the healthcare system. Besides, many recent studies point at the high reliability of cognitive screening tools at detecting and even predicting neurodegenerative diseases at their preclinical stages, when classical clinical symptoms are not yet visible and affected people are not suspected to be developing a pathological condition.

These observations are particularly relevant for Alzheimer's disease (AD), the most prevalent type of dementia among the elderly (Niu et al., 2017; Trevisan et al., 2019). Except for its early-onset familial variant, accounting for between 1% and 6% of all cases (Bird 2008), AD is typically preceded by a pre-clinical stage, which may last for more than a decade (Sperling et al., 2011), even up to 20 years (Masters et al., 2015). An important part of this pre-clinical stage falls within an MCI condition, which is usually described as an intermediate stage between normal aging and dementia (Jongsiriyanyong and Limpawattana 2018). It is estimated that up to 20% (Roberts and Knopman 2013) or even up to 25% (Jongsiriyanyong and Limpawattana 2018) of the elderly develop MCI and, from these, an important proportion – between 10% and 15% (Ataollahi Eshkoor et al. 2015) – can evolve into AD. Currently, there are no clear criteria for differentiating MCI that would progress to dementia from MCI that would not. There is no known cure for AD and both scientists and clinicians agree in that the most effective confronting of AD goes through early, preclinical detection of dementia, which would allow for more successful cognitive and pharmacological treatment of effects on different cognitive and social aspects of life. Identifying the probability of evolving to AD already at MCI stage would be the best solution.

Research is not consistent about the reliability of biomarkers for detecting MCI linked to AD (cf. Van Giau et al. 2019), although some of them defend the soundness of screening by PET (Quaranta et al., 2018), a costly and not always available technique, and SPECT perfusion neuroimaging (Henderson 2012). Using biomarkers for detecting preclinical AD was highlighted as an important solution, but the absence of clinical symptoms and signs of the disease (Dubois et al., 2016) at this stage can make it challenging for clinicians, who would have to decide whom to apply biomarkers measurements. Also, there are several established biomarkers, which allow to associate the progression from MCI to AD, like amyloid-positive PET scan, abnormal CSF tau levels, positive PET scan for tau deposition and apolipoprotein E4 genotype (Jongsiriyanyong and Limpawattana 2018). However, these clinical biomarkers are hardly detectable until prodromal AD, and some of them may also be present in elderly people without dementia who will not necessarily evolve to AD (Sperling et al., 2011; Kern et al., 2018). Some studies proposed that cognitive tests, like episodic memory screening, are potentially very useful markers of MCI progression to AD, especially when accompanying functional brain measurement (Quaranta et al., 2018) or when analyzed in correlation with previous functional screening (Marra et al., 2011). However, not all studies found significant correlation between neuropsychological and biological markers in progressing to dementia (Haldenwanger et al., 2010).

1.2. Speech assessment for early discrimination of Alzheimer's disease

In this light, one of the most promising approaches to discriminate between non degenerative MCI (nodMCI) and MCI which will evolve to dementia (preAD) is based on speech assessment. Speech is a complex physiological and neurocognitive process, which may be altered by atypical neurodevelopment and pathological processes. Physiologically, speech production represents a complex motor behavior that requires accurate coordination of the articulators and of the parts forming the human vocal apparatus (Chrabaszcz et al., 2019), being the most relevant of them the larynx, responsible for sound source, and the vocal-tract airways, acting as sound filters (Ghazanfar and Rendall 2008). The functioning of human vocal apparatus is controlled by both specific motor areas and neuroanatomical substrates for language and speech, which represent low-level and high-level processes, respectively. The speech production system is intrinsically mediated by areas responsible for neurological motor control (Hodgson and Hudson 2018), which specifically highlight the role of sensorimotor circuits in speech motor control. Rong et al. (2018) mention a complex network involved in speech production that includes medial and lateral premotor cortex, precentral and postcentral gyri, posterior inferior frontal gyrus and superior temporal gyrus, anterior insula and posterior planum temporale region, also involving portions of cerebellum and basal ganglia. Hickok (2009) refers to the left posterior sensory-related cortex as the basis of language-mediated speech production. In describing the articulatory-phonological network that allows speech production, Sörös et al. (2011) include the primary motor complex, supplementary motor area, cingulate motor area, thalamus, globus pallidus and putamen for articulation; bilateral superior temporal gyrus for phonological processing; bilateral cerebellar hemispheres for sequential movements and bilateral temporal cortex for complex phonological processing.

As a neurocognitive and motor process, speech production is highly susceptible to changes in human neural system. Hickok (2012) proposed a computational neuroanatomical model of speech production, which considers speech as both a psycholinguistic and a motor control pathway. Speech follows a psycholinguistic pathway, which allows for phoneme selection and combination in articulating lexical and discourse units on the basis of lemma choice. It also follows a hierarchical motor control pathway, which allows for correct identification, control and reaction to speech input. Different neural markers are systematically related to different speech disorders, either at the developmental stage (for example, developmental speech disorders (Morgan et al., 2018)), during the lifespan (for example, apraxia of speech (Dronkers and Ogar 2004)), or in different aging conditions.

Concerning the elderly, significant changes in speech production are found in both healthy and pathological aging. In a very recent review of speech changes in healthy aging, Tucker et al. (2021) mention as characteristics of non-pathological elderly a decrease in speech rate, an increase in significant variability in F0 and general changes in formants, a reduction of harmonic-noise ratio, an increase in jitter and shimmer, and an enlargement of segment duration and amplitude perturbation. Other recent studies on speech in healthy aging observed a stunting of the reading pace and an increase in speech errors prevalence (Gollan and Goldrick 2019). Changes in speech in the elderly are not only related to such physiological changes as decline in oro-facial motor control (Sörös et al., 2011) or muscular endurance (Bilodeau-Mercure and Tremblay 2016), but also to an impairment in the language system, specifically at the phonological level, and in general cortical sensorimotor systems involved in speech control (Tremblay et al., 2019). There is a consistent evidence that difficulties with lexical access in elderly people also play an important role in modifying speech parameters in aging (Mortensen et al., 2006).

Pathological aging, specially the one related to neurological diseases and, mainly, to dementia, also presents with important speech production changes. In addition to non-pathological neurophysiological changes in motor and cognitive control involved in speech alteration in normal aging, neuropathological processes in specific components of neural networks may be associated with different changes in speech production (cf. Wilson et al., 2010). In some cases, speech changes may exhibit very high levels of sensitivity for the diagnosis of neurological diseases. Subtle changes in speech prior to clinical diagnosis were observed for Huntington's disease, which can preclinically exhibit reduced speech agility, reduced vocal fold control, and varied speech-timing (Chan et al., 2019) due to the larger gray matter in different cortical and subcortical areas (cf. Skodda et al., 2016). Another common neurodegenerative process, Parkinson's disease, is defined by an increase in speech monotony, a decrease in tone and intensity, inappropriateness in pauses, and prosodic poverty due to dysregulation in basal ganglia (Martínez-Sánchez 2010), which participate in motor planning, programming and execution of speech (Rusz et al., 2015). Similarly, specific speech patterns like reduced speech rate and accuracy, prolonged intervals and short phrases production are suggested to be relevant for profiling the behavioral variant of frontotemporal dementia (Vogel et al., 2017).

In this respect, Alzheimer's disease, and MCI as its highly probable precursor, are currently in the spotlight of studies on speech changes driven by neurodegenerative processes. Neuropathological underpinning of AD is responsible for important impairment of semantic knowledge, which in turn drives phonological and speech errors (Forbes-McKay et al., 2013). Interestingly, it is suggested that some variation in speech production already occurs at MCI level, allowing early detection of cognitive impairment (Sanborn et al., 2020). Some of such variation can be even reliably detectable at mild stages of AD when compared with healthy speakers (Hoffmann et al., 2010).

1.3. Scope and contribution of the present research

In the present paper, we aim at focusing on describing speech changes in MCI and AD that would allow us to detect pathological processes prior to the clinical manifestation of dementia. As AD can share clinical symptoms with different types of dementia and other disorders, and frequent mixed pathologies may make it more difficult to identify it correctly (Robinson et al., 2017), we will first identify the most salient speech parameters defining AD and, presumably, MCI due to AD. To do so, we will build on our previous research in automatic speech analysis in people with dementia, as well as on studies from other specialists in the field. As an emerging field of research, automatic speech analysis is currently being explored as the best – non-invasive, reliable and economic – technique for discriminating and even predicting dementia onset and its development in the elderly. We will review the most important contributions of automatic speech analysis to the early diagnosis of AD. After that, we will propose a protocol for assessing speech parameters in AD, which will be complemented by a corpus of recordings from elderly people with different cognitive profiles (HA, MCI and AD), annexed to the present paper. It is our purpose to offer this databank of recordings to the scientific community working on speech assessment in dementia. This corpus of recordings of a standardized reading task performed by elderly people with HA, MCI and AD in Spanish is the main contribution of our paper: it is the first corpus of such characteristics for the Spanish language. Reading corpora offer an extraordinary useful type of data for automatic speech analysis, which currently makes one of the most promising technique in preclinical assessment of AD. We will conclude our paper with some comments on speech-based assessment of AD with regard to the use of automatic speech analysis, the speech corpus creation and the integration of speech impairments in the theoretical models of language competence during the lifespan. We believe that our research could additionally benefit clinical practice, since primary prevention strategies in the non-symptomatic population may result tedious because of the lack of necessary primary alarms. There is a patent need to implement a program of analyzing AD biomarkers in cognitively healthy elderly people and introducing yet not established longitudinal trials for early detection of possible and prodromal dementia (Crous-Bou et al., 2017).

2. Speech variables as biomarkers of Alzheimer's disease

Although memory impairment is still considered as a clinical hallmark of AD, studies from the past two decades highlighted the importance of language and speech traits as early, even prodromal, symptoms of dementia and pathological aging. Language is a high cognitive function with strong reliance on memory systems, and speech is a sensorimotor function with strong dependance on language architecture. Memory impairment in AD leads to early changes in codification and lexical-semantic access. As a result, speakers with AD frequently exhibit naming deficits (Fraser et al., 2016), difficulties with verbal fluency, and semantic categorization (Weintraub et al., 2012). Lexical-semantic deficits as language hallmarks of AD reflect impairments in the structure and content of semantic memory which supports language and gets disrupted as a result of pathological processes in frontal, temporal and parietal association cortices (Weintraub et al., 2012).

Some language and speech traits can already be detected in prodromal stages of AD (Ahmed et al., 2013) and, though to a lesser degree, in MCI. Significant changes in language may be observed in two thirds of the elderly one year prior to clinical diagnosis of AD (Ahmed et al., 2013), and AD-related MCI (preAD) is suggested to coincide in language deterioration pattern with AD because of parallel affection of cognitive, speech and language-related brain areas (Orimaye et al., 2018). Several studies observed that MCI individuals with impairment in multiple domains including language have a higher probability to develop AD (Taler and Phillips 2008), and that several semantic impairment properties are already detectable in MCI and preclinical AD (Cuetos et al., 2007; Venneri et al., 2016), even at early MCI stages (Mueller et al., 2018). Effects of these semantic impairments on speech may be detected in the earliest stages of cognitive decline since speech production necessarily involves recruitment of different types of memory, giving rise to observable changes, like reduction in information content, impaired fluency, changes in syntactic complexity or semantic content (Fraser et al., 2019).

The impairment in semantic and working memory plays an important role in speech organization in the elderly. Disruption of semantic components may lead to the disruption of the phonological representation of the words (Patterson et al., 1994a) and, inversely, problems with access to the phonological forms of the words may give rise to semantic errors in AD (Moreaud et al., 2001). In fact, neurodegenerative processes underlying AD do not only disrupt semantic representations, but also interfere in speaker's control over phonological retrieval, giving rise to phonemic errors and errors in lexical-phonological output (cf. Isella et al., 2020).

With this in view, recent research on discriminating MCI due to AD from non-pathological MCI has been focusing on speech traits of neurodegenerative processes. In what follows, we use two denominators – nodMCI and preAD – for referring to two general conditions of MCI subject to speech assessment. In both cases, Mild Cognitive Impairment is in course, but, unlike nodMCI, which is due to non-degenerative age-related causes, preAD shows cognitive declining due to underlying neurodegenerative processes (Hamilton et al., 2020). When the term MCI is solely used, it refers to the global condition of cognitive impairment, with no internal subdivision into nodMCI and preAD.

Concerning preAD, studies suggest that semantic disruption drives speech changes but, unlike semantic components, which may be highly modulated by the individual characteristics of the person, speech variables are usually relatively stable across speakers of the same language. Speech variables may usually be explored from three angles: acoustic, temporal and prosodic. Acoustic variables refer to the physical components defining phonemic differentiation (for example, /p/ and /b/ are steadily distinguishable because of early voicing in /b/ against the voiceless realization in the onset of /p/), and these properties are considered to be extremely relevant for correct intelligibility of speech (cf. Krause and Braida 2004). Temporal properties are a type of acoustic variables, which define the duration of phonetic segments, like sounds or syllables, and they are argued to play an important role in understanding spoken language (Greenberg et al., 2003). Finally, prosodic properties refer to suprasegmental characteristics of speech, like pitch, intonation or rhythm, which can point at syllable prominence. Some of these features can act as early biomarkers of preAD, correlating with Mini-Mental State Examination (MMSE) scores in cognitive decline (Fu et al., 2020). Together, acoustic, temporal and prosodic markers define how speech sound is dynamically organized and structured from sensorimotor and cognitive control centers, even if these patterns are imperceptible to human ear.

The main findings about speech alterations in AD reflect slower phonation and a general increase in hesitation and pauses in speakers undergoing neurodegenerative process. Semantic-based tasks, which imply overload on semantic memory and lexical access, proved to be revealing about how acoustic, temporal and prosodic parameters of guided language production can identify preclinical and clinical profiles of AD. Roughly, progression to AD is defined by a reduction in key temporal properties and a parallel increase in temporal interruptions in speech. Speech rate, which corresponds to the number of phonemes produced per second, gets significantly reduced in narrative discourse with the progress of AD (Hoffmann et al., 2010). The increase in hesitation ratio (i.e., the time between articulation and sounding), also proves to be a highly reliable temporal parameter, which allows us to discriminate not only between healthy elderly and AD speakers, but also between different AD stages: mild, moderate and severe (Hoffmann et al., 2010). The progression from non-pathological aging to MCI and AD induces more frequent pauses with larger (and more variable) duration (Pastoriza-Domínguez et al., 2021). Average duration of silent segments is argued to exhibit the highest correlation with the cognitive performance in healthy speakers, MCI and AD groups (Qiao et al., 2020). Importantly, speech alterations are already present in MCI when compared to healthy speakers. Speakers with MCI exhibit weaker voice than healthy elderly people due to increased dysphonia and an increased relation between the amplitude of the first harmonic and the amplitude of F3 (H1-A3) in phonation (Themistocleous et al., 2020), similarly to what AD speakers do when compared with healthy speakers (Tanaka et al., 2017). MCI speakers also produce longer syllables and show reduced articulation and speech rate (Themistocleous et al., 2020).

Most experimental studies on speech assessment for the early detection of AD and preAD are based on speech production elicited by picture-description tasks solely (Hoffmann et al., 2010; Qiao et al., 2020; Pastoriza-Domínguez et al., 2021) or in combination with other fluency tasks, like countdown, repetition and semantic fluency (König et al., 2015). Picture description tasks prove high reliability for lexical-semantic and syntactic discrimination between healthy elderly and AD at different stages, including the early stage of dementia (Forbes-McKay and Venneri 2005). There are important advantages in using elicited speech production, although methodological shortcomings can be easily identified. In this regard, a recent systematic review from Slegers et al. (2018) concluded that the results from different studies using picture-description tasks are conflicting for speech variables and that general cognitive heterogeneity among speakers would not necessarily produce a reliable pattern for speech-based discrimination of AD. For example, speech rate resulting from a picture-description task does not prove reliable enough for clinical research, although, as a variable, it shows significant differentiation between healthy speakers and AD. In the same way, non-unified language production (although speakers describe the same picture, their discourse production may be extremely variable) is difficult to assess through automated analysis. As a lexical-semantic-oriented test, picture description may produce highly variable results in speakers, as it occurs, for example, with verbal fluency, in which dimensions are directly dependent on specific word-finding solutions with no possible compensation. Partially controlled elicitation tasks, like picture description, may also show methodological shortcuts, like the briefness of obtained language data (Fraser et al., 2016) or an increased difficulty to analyze, *verbatim*, the produced discourse emissions (Slegers et al., 2018). In sum, in their recent review of elicitation tasks for speech assessment in AD, Boschi et al. (2017) concluded that picture-description tasks may be more suitable for analyzing lexical-semantic impairments and that, generally, semi-structured induced speech samples (interviews and story narration) are more appropriate for assessing language domains (morphosyntax and discourse). Likewise, using picture-description tasks does not always prove sensitive for MCI speakers (Taler and Phillips 2008), since speakers at early stages of AD, even at MCI, may apply compensatory strategies concealing ongoing language impairment (Ivanova 2020).

Although there have been serious attempts to automate language-based analysis for detecting MCI and AD and , specifically, for predicting MCI conversion to AD (Orimaye et al., 2018), language variability among speakers may be challenging for automatization of speech analysis. In the following section, we describe the results on the speech traits of AD and preAD based on a standardized reading task. tWe argue that the results of a reading task may turn out to be more uniform and, thus, more easily adjustable to automatic preclinical discrimination.

3. Reading-based protocol for speech assessment in Alzheimer's disease

As a cognitive task, reading can offer highly valuable information for early discrimination among nodMCI and preAD. Speakers with AD have been argued to preserve reading ability because of its high degree of automatization as a process. Even though speakers with moderate and severe AD can show reading disfluencies, reading ability is usually preserved across all stages, with the sole diminishing in the extension of the utterances AD speakers can read (Martínez-Sánchez et al., 2013). Applying three-component model of reading, Noble et al. (2000) found out that semantic disruptions in AD do not cause disruptions in orthographic and/or phonological processing during reading, as they do in other neurodegenerative diseases, like semantic dementia.

Nonetheless, recent studies suggest that some questions about reading aloud must be considered when assessing linguistic traits of AD. Though several decades ago Cummings et al. (1986) showed that reading aloud itself is a preserved ability in AD against impaired reading with comprehension, several new studies show that oral reading highly depends on the lexical and semantic characteristics of the stimuli. For example, Patterson et al. (1994b) showed that, as a type of speech elicitation task, reading aloud correlates with impairment in semantic memory and leads to reading errors when producing low-frequent and irregular words. It is, thus, suggested that oral reading significantly depends on semantic memory, involving such key variables as word regularity, frequency and imageability (Weekes 2010).

In addition to this, although the severity of AD can be traced in reading through impairment in semantic knowledge, the alteration in speech parameters is also due to an impairment at the phonological level, as showed by Colombo et al. (2004). AD development magnifies the decline in speakers' ability to monitor speech planning in the reading of upcoming speech stimuli (Gollan et al., 2020). For this, reading aloud can rapidly elicit naturalistic production of connected speech (Gollan and Goldrick 2019). Reading-based assessment in AD shows significant speech impairment as manifested by slowness of speech and articulation rate and by an increase in silent pauses and dysfluency, with speech chunking as a highly informative marker already at MCI level (De Looze et al. 2018). Our own research on speech assessment of healthy speakers, MCI speakers and speakers with AD based on read-aloud tasks allowed us to obtain reliable speech variables for early discrimination of the three groups. In this respect, it is becoming more evident that long reading stimuli (sentences or paragraphs) can be more useful in AD discriminating reading tasks. Reading of single, listed words does not allow to observe functional reading behaviors in speakers (Bourgeois 2001), while reading sequential stimuli can provide important data on semantic underlying disruption. For example, Fernández et al. (2014) observed that sentence reading can evidence the effect of working and retrieval memory impairment on a continuous contextualized task.

3.1. Participants and procedure

In the past years, we assessed several hundreds of participants with different cognitive profiles (Appendix B). All participants met the inclusion criteria: age over 60; normal vision and hearing; being a native speaker of European Spanish; a minimum of six years of primary education, for assuring literacy and easy reading of the target text with no extra cognitive load; no clinical history of head injury, depression or psychosis; no medical record of drugs or alcohol consumption; not being under pharmacological treatment affecting cognitive functions.

All participants underwent previous neuropsychological evaluation including a complete anamnesis, evaluation of daily life activities, as well as psychological and cognitive assessment through Neuronorma Screening Test (Peña Casanova et al., 2009) and Goldberg Test for depression discrimination. All participants, or their legal representatives, signed a written informed consent prior to participating in the research.

The procedure for speech assessment included a reading task embedded within the battery of other language-oriented evaluation tests. The reading task itself is based on the first paragraph (126 syllables) of the world-renowned novel by Miguel de Cervantes, *The Ingenious Gentlemen Don Quixote of La Mancha* (Appendix A), a passage well known by Spanish speakers since it represents one of the most emblematic literary works in this language. The selected text combines several characteristics. On the one hand, many speakers could reproduce it by heart, especially the beginning of the text, which already forms part of the encyclopedic knowledge of the European Spanish society. On the other hand, the text combines high-frequent terms (*salad, cloth, shoes*) and low-frequent terms (*lancerack, buckler, hack*), many of which are semantically specific (*lentils, greyhound, marketplace*) and form syntactically complex utterances including relative propositions, complex subjects and objects, and an evident sentence nominalization. In this way, the text allows us to control for semantic load, which is important for speech control and monitoring, especially in the second part of the text which is less familiar to the speakers. In this respect, the text includes very familiar elements and highly non-familiar elements, responsible for strained fluency.

In choosing this text, we refer to previous studies suggesting that reading aloud is not affected in AD for words with high-frequency and regular spelling, but that it is not spared for words with low-frequency and irregular spelling (Benigas and Bourgeois 2011). Irregular spelling-sound correspondences do not apply to Spanish, since they do not exist in this language (Cuetos et al., 2003). Considering that conversion from MCI to AD is related to the slowing of word identification during reading (Massoud et al., 2002), we assume that the combination of well-known and less-known words in the same text may convert it a very useful tool highlighting lexical and semantic underlying impairments due to neurodegeneration. The whole text is familiar to the readers and, as we previously suggested (Meilán et al., 2014), this fact allows to maintain the prosodic consistency of the reading task from the beginning to the end. As a result, high and low frequency of words is the only variable conditioning speech production on the basis of the selected text.

Reading the paragraph takes between 25 and 45 s. All participants read the text in 48-point size from a screen in a soundproof room. Microphone (20 Hz-20 kHz frequency range; 2.5 mV/Pa sensitivity; 600 ohms impedance) is placed between 8 and 14 cm from the mouth of the participant at an approximate angle of 45° in order to minimize breathe noise. Experimental terms are standardized to the maximum in order to assure equal conditions for data collection: isolated room; no background noise; same apparatus used with all participants; recording in *mono*; identical recording technique with all participants. This is particularly important in speech analysis, since some variables (like *intensity*, which values can depend on physical distance from the microphone) can be highly affected by variations in experimental (and even individual) conditions. All recordings are analyzed in Praat software, designed by Boersma & Weenink (Boersma 2001).

All participants are controlled for differences in age, sex or years of schooling. Based on the results from their neuropsychological and cognitive evaluation, participants are divided into: (a.) healthy controls ($n = 197$); (b.) speakers with MCI ($n = 91$) and (c.) AD speakers ($n = 74$). In our last reported analysis (Meilán et al., 2020), the MCI group is divided into nondegenerative MCI (nodMCI, $n = 73$) and preclinical AD (preAD, $n = 13$), and we report about the obtained results accordingly. Before taking part in the reading experiment, all participants (or their legal representatives) are informed about the test and sign the consent form in accordance with the protocol approved by the Bioethics Committee of the University of Salamanca, where all recordings were conducted.

3.2. Speech variables

Acoustic analysis of the reading task highlights several speech variables that allow us to reliably discriminate between the experimental groups.

3.2.1. Healthy elderly speakers versus speakers with mild AD

As reported in Martínez-Sánchez et al. (2013), Meilán et al. (2014) and Martínez-Sánchez et al. (2017), speakers with mild AD (GDS = 4; Global Deterioration Scale) showed significant duration, fluency, acoustic and rhythmic differences when compared with healthy elderly. Speakers with mild AD spend significantly more time on speech production and phonation; they produce significantly more pauses in number and proportion, and do so at lower elocution and articulation rates. When compared with healthy elderly, speakers with mild AD also produce syllables with longer average duration and exhibit irregular duration between syllabic intervals. They also show a significant standard deviation of the duration of syllabic intervals, which allows us to discriminate between both groups with a high level of sensitivity and specificity (over 0.8). Their speech contains more voice periods, and presents stronger fluctuation of the amplitude of sound (shimmer apq3) and a smaller noise-to-harmonics ratio (dB). Overall, mild AD speakers are slower in their speech production in reading, and, as reported in Meilán et al. (2014; 2018), usually show a higher percentage of voice breaks.

3.2.2. Speakers with nondegenerative MCI versus preclinical AD

As reported in Meilán et al. (2020), nodMCI and preAD may be discriminated based on duration, rhythm, fluency, intensity and acoustic parameters. Concerning temporal aspects, speakers with preclinical AD exhibit significantly longer duration of reading and phonation time. Their reading includes a greater number of pauses and syllabus intervals, and a higher variation in duration between two successive syllabic intervals (n_PVI). In acoustics, preclinical AD elderly show lower asymmetry (that is, a displacement of the center of gravity in frequencies towards higher frequency strip) and higher variability in the spectral area concentrating energy, as well as lower speech energy across frequency (LTAS, dB) indicating dysphony, especially in women. Gender differences are also important regarding discrimination through intensity parameters, with women with preclinical AD showing a lower mean intensity value than those of the healthy group. Overall, when compared to nodMCI, preAD elderly take it longer to read the same number of syllables and words, spending more time on phonation and including more pauses in their speech. Preclinical AD speakers vocalize more syllabic intervals but also stammer more and produce more imprecise utterances, exhibiting greater variability in the number of syllabic boundaries and in rhythm.

3.2.3. Healthy elderly speakers versus MCI versus mild AD

As reported in between-group comparison in Meilán et al. (2018), speakers with AD significantly differ from MCI and healthy groups in temporal and acoustic parameters. AD speakers show higher unvoiced percentage (time without any voiced sound) and voice breaks, and exhibit a disturbance ratio of lower intensity, as measured through 11-point Amplitude Perturbation Quotient (Shimmer apq11). Speakers with AD also show higher average variability in SD of the third formant (F3sd) when compared to both HA and MCI.

Table 1
Discriminating speech parameters for healthy controls (HC), nondegenerative MCI (nodMCI), preclinical AD (preAD) and AD.

Speech variable	HC	(SD)	*MCI **(SD)				AD	(SD)	Source
			nodMCI	(SD)	preAD	(SD)			
Acoustic Voice Quality Parameters									
Shimmer Apq11	16.20	(4.15)		*14.07	**(3.39)		13.40	(4.44)	Meilán et al. (2018)
Spectral analysis									
Assymetry (skewness, Hz)	10.05	(4.41)					8.57	(4.01)	Martínez-Sánchez et al. (2018)
			11.33	(4.14)	8.62	(4.38)			Meilán et al. (2020)
Center of gravity SD			547	(191)	753	(318)			Meilán et al. (2020)
LTAS mean (dB)			32.46	(2.31)	30.20	(2.00)			Meilán et al. (2020)
LTAS SD (dB)			40.32	(2.10)	38.16	(2.82)			Meilán et al. (2020)
Intensity									
Intensity mean (dB)			75.36	(1.77)	73.63	(2.00)			Meilán et al. (2020)
Speech fluency and rhythm parameters									
Normalized_PVI	55.55	(5.31)					60.58	(7.52)	Martínez-Sánchez et al. (2018)
			54.27	(5.42)	59.97	(5.76)			Meilán et al. (2020)
Syll_Interv_Standard	0.08–0.09	(0.00–0.01)					0.11	(0.01–0.02)	Martínez-Sánchez et al. (2017)
			0.10	(0.02)	0.11	(0.02)			Meilán et al. (2020)
Syllabus interval number			154.01	(51.88)	178.08	(33.94)			Meilán et al. (2020)
Duration parameters									
Duration (reading time)	46.02	(21.08)					76.61	(48.96)	Martínez-Sánchez et al. (2013)
			47.48	(22.20)	61.74	(20.95)			Meilán et al. (2020)
Phonation time (*sec*)	34.36	(12.21)					43.54	(18.96)	Martínez-Sánchez et al. (2013)
			32.35	(10.39)	39.44	(8.75)			Meilán et al. (2020)
Pauses number	16.51	(12.01)					33.26	(24.49)	Martínez-Sánchez et al. (2013)
			25.79	(16.34)	34.23	(14.64)			Meilán et al. (2020)
Interruption of sound									
Percentage of unvoiced segments	33.20	(8.89)		*36.52	**(9.37)		44.92 (12.68)		Meilán et al. (2018)
Percentage of voice breaks	36.84	(9.40)		*39.66	**(9.64)		48.36 (12.68)		Meilán et al. (2018)

These data show that the alteration in speech parameters that takes place throughout the evolution from healthy aging to AD follows a steady pattern parallel to the cognitive decline. Such pattern consists of a significant increase in duration in reading time and phonation, a significant extension of pauses and voice breaks, the intensification of variation in syllabic production, a decrease in speech energy and intensity, and general dysphony. Therefore, progression to AD implies conversion to slower and less intensive speech without inflection, monotone and tremulous voice, and continuous interruptions and breaks. As a result, the speech signal becomes progressively degraded and the speech itself loses clarity (Ivanova et al., 2018).

Table 1 summarizes data reported in the studies cited above (Martínez-Sánchez et al., 2013; 2017; Meilán et al., 2014; 2018; 2020).

Finally, we would like to make some comments on how the speech parameters given in Table 1 differ from phonetic changes associated to healthy aging. Indeed, non-pathological aging is characterized by alterations in speech due to complex and dynamic reorganization of neural networks supporting speech production (Sörös et al., 2011). As a result, healthy older adults share some speech traits found in pathological aging: greater airflow during speech production and slower articulation movements (Kuruvilla-Dugdale et al., 2020), driving slower speech rate, longer segment duration and more pauses (Tucker et al., 2021). Other variables, however, evolve in opposite direction when compared with AD: phonation time is shorter in healthy aging (Kuruvilla-Dugdale et al., 2020) but larger in dementia; shimmer increases in healthy aging (Das et al., 2013) but decreases in dementia; spectral center of gravity decreases for some segments in healthy aging (Taylor et al., 2020) but increases in dementia, and spectral skewness increases in healthy aging (Taylor et al., 2020) but decreases in dementia. These data may be very useful for further exploration of which linguistic traits of AD are specific to dementia and which ones replicate linguistics traits of healthy aging with a difference of degree.

3.3. *Corpus of standardized reading samples for speech assessment in MCI and AD*

As a complementary material to this paper, we offer a free-access speech corpus of standardized reading samples produced by healthy elderly, speakers with MCI and speakers with mild AD. This is one of the key contributions of this paper since, to the best of our knowledge, there currently does not exist any reading-based corpus for the assessment of progression from HA to AD. In addition, our corpus, which is available for all analyses other scholars would like to conduct, fills an important gap existing in corpora design and development in clinical linguistics. There exist very few AD language corpora for Spanish language (we explore this question with more detail further down) and our corpus aims at offering a new tool for cross-sectional study of speech and language impairments in dementia.

This speech corpus makes an extensive database of recordings of oral speech productions, noted for cognitive and social variables (MMSE, age and sex), which can be accessed, checked and used for exploring new research hypotheses. By now, only few corpora of speech production in pathological elderly are available. The most representative examples are the Dementia Bank, which includes 12 corpora for different languages (available at https://dementia.talkbank.org/), and the Carolinas Conversations Collection (CCC) (https://carolinaconversations.musc.edu/ccc/about/). Recent attempts have also been made through The ADReSS Challenge (Alzheimer's Dementia Recognition through Spontaneous Speech) (Luz et al., 2020) and Prompt Database (Rodrigues Makiuchi et al. 2020). Importantly, almost none of them -except for the Dementia Bank- includes extensive language and speech data for Spanish language. It is not yet clear to which extent language and speech impairment in aging and AD are universal across languages and exploring Spanish-based data could be likewise fruitful in this respect.

Language corpora can make a very useful tool for studying clinical pictures. More and more researchers underline the role of corpora in studying language from biomedical and clinical perspectives (for example, Roberts et al., 2009). The particular usefulness of corpora in clinical linguistics and psycholinguistics is the facility they give for computed-based analysis (Atkins and Harvey 2010). Regarding corpora for early discrimination of healthy elderly, MCI and AD, several important attempts have been made in the fields of clinical linguistics, psycholinguistics and neuropsychology. Most language database for comparing and discriminating neurocognitive pictures in aging are set on tasks eliciting spontaneous or guided (semi-structured) language production. One of the mostly used task for language elicitation in dementia, specifically AD, is the description of the *Cookie-theft picture* from the Boston Diagnostic Aphasia Examination Battery. Its systematic use and replication across studies on language in dementias has already given rise to such influential corpora as the DementiaBank (https://dementia.talkbank.org/), coordinated by Brian MacWhinney within the global project of the TalkBank (cf. MacWhinney et al., 2011 for more details on the corpus). There is a consistent defense of the importance of language data that the *Cookie-theft picture* can provide to clinicians with respect to different language competences (semantics, pragmatics or discourse) (see Cummings 2019 for a discussion on the utility of this test for detection of AD), but there is still no standardized design for the inclusion of this test in quick and early assessment of cognitive and language conditions.

Important intents have been made in computational sphere in order to automatize the analysis of spontaneous and guided language production for early detection of AD. These intents mainly combine *natural language processing*, a set of computer systems able to analyze, understand and reproduce human languages (Allen 2003), and *machine learning*, a computational technique allowing to engineer mathematical models able to determine probabilities distributions on the basis of statistical learning (Bonaccorso 2017). *Cookie-theft picture* is among the most tested tasks for machine learning automatization. With respect to it, transformer models have been applied for machine assessment of discourse production for classifying speakers into healthy or AD group. For example, a transformer model known as BERT (*Bidirectional Encoder Representations from Transformers*) was applied by Wahlforss & Aslaksen Jonasson (2020) and allowed them to discriminate between control and AD groups with an accuracy of 90% by analyzing transcripts of *Cookie-theft picture* description generated by automatic speech recognition system. Furthermore, de la Fuente García et al. (2019) recently applied machine learning algorithm to the analysis of a novel model of linguistic data for early detection of dementia based on dialogue features. In an innovative way, these authors develop on the PREVENT Dementia dataset in order to establish correlations between conversation-based features and progression of AD.

Concerning Spanish language, very few corpora have been collected for MCI and AD. Among such, we can mention the PerLA corpus (https://www.uv.es/perla/CorpusPerla.htm), coordinated by Professor Beatriz Gallardo-Paúls in the University of Valencia for different types of aphasias and based on spontaneous interviews. It is not yet clear whether speech and language alterations in neurodegenerative diseases are universal across languages or whether they exhibit variation according to their structural specificity. The need to rely on more corpora based on data from languages other than English is, thus, outstanding in order to detect and propose sensitive speech and language classifier for speakers of different languages (Li et al., 2019).

Corpora based on reading stimuli may be particularly distinguished for their utility in speech- and language-based clinical diagnosis. Unlike open corpora based on freely-produced discourse, which can lead to underrepresentation of important disease-related patterns in quantitative examination (cf. Atkins and Harvey 2010 for an overview), corpora based on standardized stimuli allow to design comprehensive algorithms for automated analysis. In this type of corpora no tagging is needed, since automated analysis follows probabilistic statistical principles (Ferguson et al., 2009). In particular, when comparing classification accuracies across different tests, they get higher scores from reading-based stimuli than from language elicitation stimuli. While *Cookie-theft picture* analysis can show a classification accuracy between healthy speakers and AD varying between 81% (Fraser et al., 2016; based on 473 samples), 82,1% (Guo et al., 2021; based on 156 samples) and 90% (Wahlforss and Aslaksen Jonasson 2020; based on 551 samples), and with 85% of classification sensitivity for HA, MCI and AD (Hernández-Domínguez et al., 2018; based on 517 samples), speech-based automated analysis can classify speakers without dementia and AD with an accuracy of 87% (Martínez-Sánchez et al., 2018; based on 145 samples), and HA, MCI and AD with an accuracy of 91,2% (Meilán et al., 2018; based on 182 samples).

4. Discussion

Neuropsychological screening tests make it difficult to discriminate between MCI speakers which would not develop pathological aging from those who will evolve to AD. Preclinical AD can be detected through clinical biomarkers tests, such as blood tests, cerebrospinal fluid analyses and brain neurophysiology observation. However, their costly and time-consuming nature can hinder the detection of AD onset prodromally. Preclinical detection of AD is highly necessary since early diagnosis is the key to successfully confronting the disease in all respects: it can allow patients to actively participate in taking decisions about their future and to get

Table 2
Metadata of reviewed studies.

	Experimental group				Source
	NPS	MCI	PreAD	AD	
MMSE (SD)	26.21 (3.80)			16.29 (7.42)	Martínez-Sánchez et al. (2013)
Sex (m/w),%	80.6/19.4			77.1/22.9	
Mean age (SD)	76.31 (12.25)			80.17 (7.43)	
MMSE (SD)	27.97 (1.15)			18.07 (3.86)	Meilán et al. (2014)
Sex (m/w),%	20/80			32/68	
Mean age (SD)	74.06 (9.74)			78.66 (9.38)	
MMSE (SD)	28.59 (1.55)			16.93 (6.64)	Martínez-Sánchez et al. (2017)
Sex (m/w),%	31.7/68.3			35.6/64.4	
Mean age (SD)	75.83 (6.22)			77.80 (9.32)	
MMSE (SD)	28.39 (1.98)	24.03 (4.02)		19.45 (6.95)	Meilán et al. (2018)
Sex (m/w),%	26.5/73.5	26.3/73.7		35.7/64.3	
Mean age (SD)	75.54 (6.44)	75.61 (7.13)		79.1 (5.52)	
MMSE (SD)	28.16 (2.24)			20.30 (6.51)	Martínez-Sánchez et al. (2018)
Sex (m/w), n	30/68			14–33	
Mean age (SD)	76.18 (6.44)			80.83 (6.39)	
MMSE (SD)		23.25 (4.63)	24.31 (4.37)		Meilán et al. (2020)
Sex (m/w),%		27/73	31/69		
Mean age (SD)		78.73 (10.07)	82.92 (5.02)		

benefits from early pharmacological treatment and cognitive stimulation, which could assure them longer functional independence and higher quality of life (Leifer 2003). In addition, the early detection of AD can provide affected persons with necessary tools for coping with the progressive cognitive and functional decline, while allowing them to seek adequate assistance from the healthcare system (Mattsson et al., 2010). In sum, an early diagnosis of the disease can guarantee a higher quality of life to the patient and their caregivers, and can reduce the cost of institutionalization and healthcare (Rasmussen and Langerman 2019).

In this paper, we aimed to offer a detailed perspective on how speech analysis based on reading tasks can contribute to the early detection of prodromal AD. AD can have a very long prodromal period and its preclinical stage may be already detected in speech when speakers seem to be on a state of/suffering from/manifesting MCI. Due to the heterogeneity of MCI profiles and their possible evolution to AD (nondegenerative MCI which will not lead to AD and MCI which will lead to AD), non-invasive assessment of the risk of evolution to AD is crucial at this stage in order to decide on whom to apply further screening and diagnostic tests to confirm the disease. Here, we described how preclinical AD can be identified through a simple standardized reading task, involving familiarity and semantic load, and its automatic analysis for acoustic, temporal and prosodic speech traits. Although picture-description tasks for elicitation of connected speech are traditionally used for further phonetic analysis in MCI and AD, we suggest that using a reading task with invariable verbal stimuli may be more convenient for the early automated assessment of the possibility of developing AD. Therefore, controlling verbal production ensures that the main source of heterogeneity comes from the cognitive state of speakers. It also allows us to obtain highly uniform language data and to avoid early-stage compensatory strategies. Importantly, unified data enable researchers and clinicians to recur to automated analysis.

The automated analysis of biological samples for the early detection of AD is one of the most sought-after solutions. The ever-increasing incidence and prevalence rates of both MCI and AD highlight the necessity to undertake large-scale screenings in the elderly, which would require quick, reliable and easily interpretable tests for detecting pathological cognitive changes. It is estimated that more than 700 million people worldwide are aged 65 or over (United Nations 2019). Age is considered to be the greatest risk factor for developing AD (Riedel et al., 2016) and it is estimated that AD prevalence oscillates between 10% and 30% in people over 65 (Masters et al., 2015). Automated analyses are absolutely necessary for early screening and diagnostic evaluation in primary care.

There were several attempts to automate speech analysis for the early detection of AD, and many of them are based on machine-learning protocols. O'Malley et al. (2020) developed a fully automated system, called *CognoSpeak*, which assesses speech properties in people with memory complaints and attain a high level of sensitivity in discriminating between healthy speakers or functional cognitive disorder group and MCI or AD (86.7%). Toth et al. (2018) used recall and question-answer stimuli to test the usefulness of an automatic-speech-recognition (ASR) -based tool and machine learning algorithms, and proved that speakers with MCI can be discriminated from healthy elderly with an accuracy (F1-score) of 78.8% on the basis of speech tempo and number of pauses in speech. König et al. (2018) developed a mobile application assessing verbal fluency through picture description, counting down and a free

Table 3
Reading corpus metadata.

Corpus metadata Total number of subjects = 361 Diagnostic group	n of subjects	MMSE (SD)	Gender	Age	Schooling years
Healthy speakers	$n = 197$	28.26 (1.890)	Men = 58, Women = 139	75.5 (7.929)	9.58 (3.848)
MCI	$n = 90$	23.89 (4.082)	Men = 25, Women = 65	79.49 (9.605)	8.67 (3.938)
Dementia	$n = 74$	19.97 (5.174)	Men = 30, Women = 44	79.49 (7.921)	8.81 (4.095)

speech task; that allowed them to discriminate between healthy speakers, MCI and AD with accuracy between 86% and 92%. Shifting the focus from speech properties to language structure/grammar, Orimaye et al. (2017) developed a machine-learning model allowing to significantly distinguish between probable AD and healthy speakers on the basis of n-gram linguistic biomarkers, syntactic components and lexical components.

Our research group also contributed to the development of the automated speech analysis techniques for the early discrimination of AD. As reported in Martínez-Sánchez et al. (2018), we developed the VAD-AD (Voice Analysis Diagnosis of Alzheimer's Disease) prototype, which assesses speech parameters produced while reading a given text, and estimates the speaker's profile: "very likely normality", "probable normality", "borderline case", "probable dementia" or "very likely dementia". The classification accuracy of VAD-AD for discriminating between healthy elderly and AD is 92.4%. It includes a complex algorithm of acoustic and temporal parameters. However, in a very recent research application of the VAD-AD, Meilán et al. (2020) found that not all included parameters are sensitive to distinguishing between nondegenerative MCI and preclinical AD. This observation suggests that speech-based automated algorithms should be specified for each progressive stage, from healthy elderly to MCI, preclinical AD and mild AD.

Consequently, we believe that recent advances in the automated assessment of probable AD should inspire new complex contributions to profiling and specifying pathological cognitive impairment. Speech variables can be very sensitive to changes in the neuropsychological state of the elderly, and therefore parametric speech profiles should be established for assessing progression from one clinical stage to another. Similarly, more longitudinal studies concerning the evolution from stage to stage are needed, and, in this respect, reading tasks may result particularly revealing since they ensure same stimuli comparison over time. Currently, reading tasks are underrepresented in automated speech assessment of progression to AD as revealed by a systematic review from Petti et al. (2020).

In order to boost future research on automatic speech analysis based on standardized reading stimuli, we annex to this paper a corpus of recordings from elderly speakers with different cognitive profiles. All speakers read the same text, consisting of the first paragraph of *The Ingenious Gentlement Don Quixote of La Mancha*, by Miguel de Cervantes. We believe that this corpus could be useful for additional exploration and creation of algorithms for the automated assessment of these different cognitive profiles. In fact, language corpora of speech production in AD already inspired several studies on automated assessment of AD. For example, the most known corpus, the Dementia Bank, was used by Fraser et al. (2016) to develop a machine-learning classifier with over 81% accuracy between possible / probable AD and healthy controls. The same corpus was used by Orimaye et al. (2017) to develop a machine-learning algorithm to enhance clinical diagnosis of probable AD. Recently, Faroqi-Shah et al. (2020) employed the Dementia Bank to automatically analyze narrative samples seeking to successfully distinguish between primary progressive aphasia (PPA), healthy aging and MCI. Definitely, language and speech corpora can be very useful for testing new discriminating and diagnostic techniques in neurodegenerative diseases.

We strongly believe that the automated analysis of speech based on reading can benefit clinical practice as a primary screening test. Certainly, speech assessment results must be validated by neuropsychological and, when possible, neurophysiological and neuroimaging tests, but their utility is undeniable for early mass screening of the elderly.

5. Conclusions

In this paper, we examine how AD can be discriminated from other cognitively impaired profiles in aging, specifically, from MCI, on the basis of automatic speech analysis of reading samples. We make an overview of the acoustic, temporal and prosodic variables of speech produced by elderly people with different cognitive profiles – from non-pathological aging to nodMCI, preAD and mild AD –, and provide the reader with free access to a corpus of reading samples from three groups: HA, MCI and AD. We conclude that standardized reading tasks can significantly benefit the accuracy of speech-based discrimination between cognitive groups and may be more convenient for developing automated analysis techniques and procedures.

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Declaration of Competing Interest

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Appendix A

Original stimulus text

En un lugar de la Mancha, de cuyo nombre no quiero acordarme, no ha mucho tiempo que vivía un hidalgo de los de lanza en astillero, adarga antigua, rocín flaco y galgo corredor. Una olla de algo más vaca que carnero, salpicón las más noches, duelos y quebrantos los sábados, lantejas los viernes, algún palomino de añadidura los domingos, consumían las tres partes de su hacienda.

Translation into English

In a village of La Mancha, the name of which I have no desire to call to mind, there lived not long since one of those gentlemen that keep a lance in the lance-rack, an old buckler, a lean hack, and a greyhound for coursing. An olla of rather more beef than mutton, a salad on most nights, scraps on Saturdays, lentils on Fridays, and a pigeon or so extra on Sundays, made away with three-quarters of his income.

Appendix B

Metadata for used materials (Table 2 and 3)

Supplementary material

Corpus of standardized reading samples for speech assessment in HA, MCI and AD. 10.1016/j.csl.2021.101341

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