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Original Research Article

Speech in Alzheimer's Disease: Can Temporal and Acoustic Parameters Discriminate Dementia?

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Key Words
Alzheimer's disease · Acoustic measures · Discriminant analysis · Speech measures

Abstract
Aims: The study explores how speech measures may be linked to language profiles in participants with Alzheimer's disease (AD) and how these profiles could distinguish AD from changes associated with normal aging. ***Methods:*** We analysed simple sentences spoken by older adults with and without AD. Spectrographic analysis of temporal and acoustic characteristics was carried out using the Praat software. ***Results:*** We found that measures of speech, such as variations in the percentage of voice breaks, number of periods of voice, number of voice breaks, shimmer (amplitude perturbation quotient), and noise-to-harmonics ratio, characterise people with AD with an accuracy of 84.8%. ***Discussion:*** These measures offer a sensitive method of assessing spontaneous speech output in AD, and they discriminate well between people with AD and healthy older adults. This method of evaluation is a promising tool for AD diagnosis and prognosis, and it could be used as a dependent measure in clinical trials.
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As early as 1907, Aloysius Alzheimer clinically described the patients with Alzheimer's disease (AD) as presenting with paraphasia, pauses in speech, and impairments in comprehension, in reading as well as in writing [1]. Indeed, he established that memory impairments in persons with AD were quantitatively different from those in other forms of pathological aging; in contrast, language impairments were qualitatively different, but still clearly characterised the disease [2]. Previously, language deficits were frequently noted in the lexico-

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semantic and pragmatic domains of language [3], while the articulatory, phonological and syntactic aspects of language production were often reported to be relatively well preserved until the severe stages of AD [4].

However, the likelihood that alterations occur in spontaneous language production has been highlighted by a classic study indicating reductions in semantic skills and sophistication of vocabulary in Iris Murdoch's last novel, published a year before her diagnosis of AD [5]. Clinical studies typically adopted a profile of early speech symptomatology in AD [6]: a lack of initiative, slowness, articulatory apraxias, excessive length of phrases and sentences, paraphasia, anomic aphasia, lack of informative content due to the use of vague and imprecise phrasing, low melodic level, and low rhythm. In recent years, more in-depth studies have been carried out of the speech disorders associated with the evolution of AD [7, 8]. Kemper et al. [9] claimed that AD is often the most common cause of logopenic progressive aphasia, which is characterised by a reduced or fluctuating rate of language output, phonological errors, and frequent word-finding pauses. The patients are still able to produce speech, but their speech rate may be significantly slowed down due to word retrieval difficulty. Logopenic progressive aphasia mostly occurs in the early stages of AD, especially in cases of early-onset AD and AD with a more rapid progression in patients with a family history of dementia [10, 11].

Some experimental studies have examined spontaneous speech in free conversations recorded from patients with AD to appraise their conversational speech. In mild AD, phonological and articulatory impairments and phonological paraphasias have been found [12], as well as slow speech [13]; the ratio between perseverative and anticipatory speech errors (anticipatory proportion) was significantly lower [14], more empty language and shorter conversational turns were observed [15], as well as higher hesitation ratios [16], and more phonological errors [17]. Tosto et al. [18] found prosodic impairment in AD: features of speech such as emphasis placed on certain syllables, changes in tempo or timing, and differences in pitch and intonation. In short, if the impairments in speech in individuals with AD differ qualitatively from those caused by normal aging or other pathologies, such impairments may be thought to serve as objective, early, subtle, clear and isolated symptoms for the early diagnosis of AD [19].

Speech processing techniques are often applied to assist in extracting information from unstructured speech. They are methods for automatically measuring speech characteristics and examine the utility of these measures for discriminating between clinically defined groups [20]. Some studies have examined spoken language samples recorded from patients with AD and mild cognitive impairment. Subtle speech alterations were revealed in a recent study indicating the difficulties in expression (e.g. percentage of voiceless segments) shown by patients with AD in the early stages of the disease [21, 22] and the difficulties in speech duration (e.g. mean duration of pauses, standardized phonation time, and verbal rate) observed in patients with mild cognitive impairment [23].

As we have seen, the most prominent speech characteristics affected by early AD are those related to prosody, temporal and acoustic measures, which includes the alterations in rhythm (reduced or fluctuating rate of language output, frequent word-finding pauses, a lack of initiative, and slowness), loudness, phonological errors, and articulatory apraxias [24]. These characteristic alterations could be detected by analysis of temporal and primary acoustic parameters: for example, temporal aspects of the speech sample and interruption of sound for alterations in rhythm; analysis of the fundamental frequency (F_0), periods of voice, and fluctuation in frequency for slowness, phonological errors and articulatory apraxias, and fluctuation in amplitude for loudness. In this study, our objectives were to identify the speech parameters in AD, to analyse the difficulties in expression shown by patients with AD in the early stages of the disease, and to study the speech profile of patients with AD.

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Our first specific aim was to take a direct and objective measure of the speech of individuals through temporal and acoustic analysis. Our hypothesis was that there are qualitative differences between the expressive language of patients with AD and that of other elderly persons with regard to prosody, voice quality, pitch, articulation, intensity, and the stability of voice. These differences would allow us to obtain a profile for AD that would enable the differential diagnosis of AD with respect to individuals without this pathology [25, 26]. We thus analysed the role of specific temporal and acoustic measures as potential early markers for the onset, progression, and severity of AD. With this goal in mind, specific sentences spoken by patients with mild AD were recorded and compared to those spoken by elderly individuals without pathology. We analysed the intensity, fundamental frequency, and the temporal structure of this speech in its suprasegmental aspects. With these findings, we performed a discriminant analysis to classify participants into AD or control groups.

Methods

Participants

We collected audio recordings from 66 participants (in two groups, a normal control group and an AD group) aged over 60 years, with no history of drug or alcohol abuse, no symptoms of depression (Beck Depression Inventory score <10) and no co-existing degenerative neurological disease or hearing impairment that could affect speech and voice production. The AD group (n = 30; mean age = 78.66 years, SD = 9.38, range 60–95; men = 32%, woman = 68%; mean years of formal education = 6.27, SD = 2,5, range 3–14) comprised patients from a National Reference Centre for Alzheimer Disease with a diagnosis of probable AD (NINCDS-ADRDA) and with a score of 4 on Reisberg's Global Deterioration Scale (patients show evidence of mild memory deficit during intensive clinical interview; MMSE corrected mean score = 18.07, SD = 3.86, range 12–23). We excluded patients with a diagnosis of mixed dementia. The MMSE score in the AD group was heterogeneous, but was controlled by the clinical aspects assessed. Our patients were in the Program for Integral Cognitive Activation in Dementias at the National Reference Centre for Alzheimer Disease, and therefore maintained a communication system, the reading ability, and the ability to follow instructions. The participants were able to do the reading task. They invariably knew their own name and the name of their spouse and children, and they could still remember significant details about themselves and their family.

The normal control group participants were healthy elderly individuals (n = 36; mean age = 74.06 years, SD = 9.74, range 60–98; men = 20%, woman = 80%; mean years of formal education = 7.30, SD = 3.1, range 4–14) recruited through education courses for the elderly at the university. They were fluent in language with no history of head injury, neurological disease, major affective or psychotic disorders, seizures, or substance abuse, and they were within normal limits on age- and education-matched cognitive tests (MMSE corrected mean score = 27.97, SD = 1.15, range 26–30).

Men and women were grouped by gender to conduct the analyses, but no significant differences were found between the two groups [$\chi^2(1) = 1.247$] with regard to age ($t_{64} = 1.923$) or mean years of formal education ($t_{64} = -1.422$). However, significant differences were observed between the two groups in MMSE mean score ($t_{64} = -13.254$; $p < 0.001$).

Materials

Audio recordings were obtained using a professional Fostex FR-2 LE recording equipment, with 24-byte resolution, a sampling rate of 48 kHz, and an AKG D3700S cardioid microphone. The microphone was placed on a stand 8 cm from the participant at an angle of 45° to the patient's mouth to decrease aerodynamic noise from the mouth. The sampling frequency rate and volume were controlled so that there was consistency among the participants. Acoustic parameters were evaluated with automated scripts written for the Praat software (version 5.1.42) [27] to extract estimates of the relevant acoustic measures from the recordings.

Procedure

All participants gave informed consent for the assessment in line with the ethical conventions of the institution. All subjects underwent a comprehensive neuropsychological assessment including measures of speech, the biographical information test, and the corrected MMSE. The speech task consisted of the partici-

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pants reading a series of familiar sentences presented on a screen, in 48-point font size and multiple lines to facilitate reading. The reading task should be easy because the participants already know the phrases to be read. They were asked to read the sentences appearing on the screen and to try to speak loudly and clearly. The acoustic analyses were done on the same segments for all of them: the participants were asked to read two well-known sentences in Spanish from *Don Quixote de la Mancha* by Miguel de Cervantes. They are the popular first sentences of the book: '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' (English translation of *Don Quixote* by John Ormsby, 1885).

Analyses focused on common acoustic measures of speech, including temporal aspects of the speech sample, pitch (F_0), volume (intensity), and voice quality. To characterise the temporal aspects of the speech sample, we computed the duration of the voice sample used (total duration of the paragraph from *Don Quixote,* the phonation time, and the reading and articulation speed), the interruption of sound (proportion and number of pauses of voice, percentage of the recording without voice, and number and percentage of voice breaks), and the periods of voice (number of pulses analysed as voice, and mean number of periods of voice). To characterise the pitch or fundamental frequency (F_0), we analysed the fundamental frequency (mean F_0, maximum and minimum values of F_0, high and low global pitch and autocorrelation measures), and fluctuations in the frequency of sound [*jitter* (short-term, cycle-to-cycle, perturbation in the fundamental frequency of the voice): local jitter, local absolute jitter, relative average perturbation jitter, and quotient 5 jitter]. To characterise the fluctuations in the amplitude of sound, we computed the intensity (in dB) of voiced and unvoiced signals, and measures of phonatory stability [period perturbation *shimmer* (short-term, cycle-to-cycle, perturbation in the amplitude of the voice): local shimmer, amplitude perturbation quotient (apq) 3 shimmer, apq5 shimmer, and apq11 shimmer]. Finally, we computed measures of the speaker's voice quality. Two spectral noise measures were calculated: the harmonics-to-noise ratio and the noise-to-harmonics ratio.

Data Analysis

The spectrographic measures used in this study were subjected to linear discriminant analysis by a step-by-step procedure described elsewhere, using diagnosis (1 = AD; 2 = control) as the dependent variable. The stepwise statistical method of linear discriminant analysis enables a subject to be assigned to a previously classified group (criterion or dependent variable) according to the scores in different independent variables, which are then linearly combined via a 'discriminant function' [28]. The objective of this technique is to select from a set of independent variables those that best discriminate between the two groups of the dependent variable, thus satisfying the criterion of parsimony and obtaining the greatest diagnostic accuracy with the minimum number of variables. The procedure of including the variables in the equation also enables the calculation of the net contribution of each variable alone. A cross-validation by resubstitution (SPSS Inc., v18) [29] was also performed.

Results

Speech Analysis

Table 1 shows the speech parameters that were measured and the descriptive data. Linear discriminant analysis results make it possible to obtain a highly significant discriminant function (percentage of variance explained = 100%; eigenvalue = 1.095, canonical correlation = 0.723; Wilks' lambda = 0.477, $\chi^2 = 45.488$, d.f. = 5, $p < 0.001$) containing 5 factors (table 2). The discriminant function, in standardised coefficients, took the following parameters into account: the total number of voice periods (SC = 0.874), breaks in voice [calculated both as a percentage of voice breaks (SC = 0.787) and voice break number (SC = –0.683)], fluctuation of the amplitude of sound as shimmer apq3 (SC = 1.381), and, finally, noise-to-harmonics ratio (SC = –1.127). Table 2 shows Wilks' lambda and Fisher coefficients of the structure matrix for each variable. The non-standardised centroids for AD are 1.129 and for the control group –0.941.

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Table 1. Measured speech parameters and descriptive data

Group	Parameters	Control (mean ± SD)	AD (mean ± SD)
Temporal aspects of the speech sample	Total duration, s	44.39±18.32	82.19±53.05
	Phonation time, s	34.30±13.21	46.72±19.86
	Speech rate, syllable/s	3.59±0.67	2.55±0.63
	Articulation rate, syllable/s	4.34±0.43	4.05±0.43
Analysis of fundamental frequency (F_0)	Mean F_0, Hz	161.27±24.48	179.08±29.05
	Minimum F_0, Hz	68.46±4.00	67.66±3.78
	Maximum F_0, Hz	542.85±124.91	596.63±68.76
	Autocorrelation, Hz	0.89±0.04	0.90±0.05
	High global pitch, Hz	478.12	571.25
	Low global pitch, Hz	76.82	82.50
Analysis of periods of voice	Pulses, n	4,221±1,834	6,520±2,872
	Periods, n	4,126±1,804	6,379±2,830
	Mean periods, n	6.38±1.05	5.76±0.88
Interruption of sound	Without voice, %	35.66±7.40	47.83±12.28
	Voice breaks, n	84.05±29.95	118.93±68.27
	Voice breaks, %	39.62±6.85	51.27±12.03
	Proportion of pauses of voice	28.67±12.887	51.76±13.55
	Pauses of voice, n	14.33±9.3	34.5±27.04
Fluctuation in frequency	Jitter (loc), %	2.83±0.61	2.80±0.95
	Jitter (loc, abs), %	182.71±54.65	165.22±75.41
	Jitter (rap), %	1.33±0.34	1.34±0.54
	Jitter (ppq5), %	1.52±0.46	1.54±0.61
Fluctuations in the amplitude of sound (intensity of sound)	Shimmer (loc), %	12.94±4.09	13.28±4.71
	Shimmer (loc), dB	1.58±0.44	1.60±0.51
	Shimmer (apq3), %	5.29±2.19	6.01±2.74
	Shimmer (apq5), %	7.77±3.07	7.92±3.43
	Shimmer (apq11), %	14.04±4.57	12.66±4.58
	Intensity of unvoiced, dB	56.62±4.38	53.27±5.15
	Intensity of voiced, dB	71.10±3.98	70.35±2.74
Harmonics/noise ratio	Noise-to-harmonics ratio, dB	0.17±0.65	0.15±0.07
	Harmonics-to-noise ratio, dB	12.43±2.86	12.72±2.64

loc = Local; loc, abs = local absolute; rap = relative average perturbation; ppq5 = 5-point period perturbation quotient.

Table 2. Wilks' lambda and Fisher coefficient structure matrix for each introduced variable

Parameters	Wilks' lambda	Structure matrix: function
Percentage of voice breaks	25.717**	0.654
Number of periods	17.940**	0.471
Number of voice breaks	14.886**	0.330
Shimmer (apq3)	13.162**	0.131
Noise-to-harmonics ratio	13.142**	–0.138

** $p < 0.001$.

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Once the discriminant function was obtained, the participants in the sample were classified according to the scores. Fifty-six of the 66 patients were correctly classified by this procedure, thus providing 84.8% sensitivity for classification. Only 6 participants in the AD group and 4 in the control group were classified incorrectly. In the cross-validation study, 55 of the 66 participants were correctly classified by this procedure, thus providing 83.3% sensitivity for classification. Seven participants in the AD group and 4 in the normal control group were classified incorrectly.

Discussion

This study reports on the ability of speech analysis to discriminate between patients with mild AD and healthy older adults. We examine a large set of temporal and acoustic measures and demonstrate that they can be useful for discriminating between healthy and AD groups. The findings suggest that speech measures may indeed be valuable for the detection of AD. The two groups performed qualitatively differently in the speech task, and the participants were divided into the disease group and the control group based upon only 5 factors: percentage of voice breaks, number of periods of voice, number of voice breaks, shimmer (apq3), and noise-to-harmonics ratio. Thus, the temporal and acoustic values analysed allow us to define the profile of individuals with AD in a valuable way.

The variables were interpreted using Fisher coefficients of the matrix structure (table 2). In our analysis of voice periods, we found that speech of the AD participants was characterised by an overall higher number of periods of sound. A period is the time it takes to complete one cycle. The number of periods is the length of time for the interval of cycles selected to analyse. This higher number of periods implied that the voice vibrated at fewer cycles per second, presenting in the AD group as a deeper voice, slower speech, and a slower rate of speed or rhythm of the glottal pulses. This gives rise to a monotone voice. Also, Horley et al. [30] found that in speech, objective acoustic measurements revealed significantly less pitch modulation by the AD group. For the interruptions of the voice, we found that the speech of the participants with AD was characterised by a higher proportion and number of voice breaks. Voice breaks are the interruptions or variations taking place along the melodic curve, not perceptible to the human ear because of their short duration. The number of voice breaks is the number of distances between consecutive pulses that are longer than 1.25 divided by the pitch floor. Voice breaks are a voice disorder wherein the pitch of the voice changes suddenly. AD speech is contaminated by these voice breaks, and characteristic noises like bubbles or tremors in the voice start to appear. Noise and voice break parameters give information regarding the amount of noise in the voice signal. In our analysis of fluctuations in the amplitude of sound, participants with AD had a higher apq. The shimmer index refers to period-to-period amplitude variation in the voice signal. It serves to quantify the small intervals of instability in the voice signal by means of a relative evaluation of the fluctuation in amplitude from one period to another (from peak to peak). Shimmer is the apq, between the amplitude of a period and the average of the amplitudes of its neighbours, divided by the average amplitude. The group with AD showed greater variations in the intensity of the successive waves produced continuously, especially in the variation of the amplitudes of their two closest neighbours (shimmer apq3). Patients with AD had a tremulous voice, with less intensity and less control of airflow than the control group.

As noted, the voice alterations that discriminate in the analysis between the two groups are related to acoustic changes characteristic of the voice of patients with AD. Because the differences between the two groups can be justified by changes in the production of phonemes or sequences of sounds, this allows us to generalise the discriminant analysis to languages

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other than English. However, these results contrast with other studies in which the emphasis is on the temporal and prosodic aspects of speech. These seem to also be altered due to disease as reported by ourselves and other authors using different methodology [13, 21, 24]. Recently, Meilán et al. [22] have found that an increase in the percentage of voiceless segments in AD patients' speech explains more than 34% of the variance in the scores in a specific language and memory test. Roark et al. [23], in a task where the participants were asked to re-tell a story (Wechsler Logical Memory Scale) immediately after it had been told to them, found that the standardised pause rate, phonation rate, and many linguistic complexity measures were useful in discriminating between healthy elderly participants and participants with mild cognitive impairment. However, Singh et al. [13] reported that the mean duration of pauses, standardised phonation time, and verbal rate were useful in discriminating between healthy elderly participants and patients with AD. The differences in the significance of speech-based markers between the authors may be due to the large number of differences between the studies, including the number of participants, inclusion criteria for the participants, test material, and measurement tools.

Our results may be a consequence of using a familiar phrase of *Don Quixote,* which allows participants to keep the prosody of the language more appropriate and consistent, highlighting that the test used altered acoustic features compared to prosodic features. The prosodic features would not discriminate when taking into account familiar prayers, but rather in tasks that use memory to search the right words. In this case, there is a difference between reading a known text and reading an unknown text that has been read only once. To conclude, it is well documented that AD patients often manifest deficits in language processing very early in the course of the disease, and a review of the performance of AD individuals in language tasks is timely and will contribute to the goal of identifying early markers of cognitive impairment in AD [31, 32]. Authors like Roark et al. [23] indicate that using multiple, complementary spoken language measures can help in the automatic detection of mild cognitive impairment. They demonstrate that effective automation of measure extraction is possible when given a transcript and audio recordings, so that significant differences in feature means between healthy and mild cognitive impairment groups are preserved.

We designed a direct method for automatically measuring language production by an objective and ecological task, which can be applied in a very short period of time. It is a method for automatically measuring the speech characteristics of spoken language samples. We have examined the usefulness of this method for discriminating between patients with early AD and controls and for obtaining a precise diagnosis of AD. These speech measures may indeed be valuable in the detection of AD. Spoken language examination is a relatively inexpensive and simple measure, and it has the additional advantage of minimal discomfort for the patient. The use of spectral analysis tools yields an objective description of the voice output, which will allow specialists to unify concepts. Cognitive processes involving both executive and lexical-semantic memory access determine the characteristics of speech. Future research should address both sources of speech failure in AD patients.

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