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Temporal parameters of spontaneous speech in Alzheimer's disease

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Abstract
This paper reports on four temporal parameters of spontaneous speech in three stages of Alzheimer's disease (mild, moderate, and severe) compared to age-matched normal controls. The analysis of the time course of speech has been shown to be a particularly sensitive neuropsychological method to investigate cognitive processes such as speech planning and production. The following parameters of speech were measured in Hungarian native-speakers with Alzheimer's disease and normal controls: articulation rate, speech tempo, hesitation ratio, and rate of grammatical errors. Results revealed significant differences in most of these speech parameters among the three Alzheimer's disease groups. Additionally, the clearest difference between the normal control group and the mild Alzheimer's disease group involved the hesitation ratio, which was significantly higher in the latter group. This parameter of speech may have diagnostic value for mild-stage Alzheimer's disease and therefore could be a useful aid in medical practice.

Keywords: *Alzheimer's disease, spontaneous speech, temporal analysis, diagnosis, phonetics.*

The nature of neuropsychological deficits in Alzheimer's disease (AD) has been intensely researched over the past few years. Research has focused on aspects of memory impairment at various stages of the disease. For the earliest stages of the disease, i.e., mild AD, it is only in recent years that the prodromal phase of neuropsychological decline in AD has come under examination (Germano & Kinsella, 2005), despite the consensus that it is important to identify clinical features of mild AD in order to have access to drug therapies that are able to modify the disease and also to develop more effective management strategies. There is a consensus among most neuropsychological studies that memory impairment, potentially associated with pathological changes in mesial temporal structures, is the earliest and the predominant cognitive deficit in AD (Fox & Rossor, 1999; Storey, Kinsella, & Slavin, 2001). However, controversies still surround the definition of mild AD concerning the precise cognitive deficits that co-exist with or underlie the memory impairment in the earliest stages of the disease (Germano & Kinsella, 2005; Storey, Slavin, & Kinsella, 2002).

In this article we investigate the temporal parameters of spontaneous speech in AD, with a special focus on identifying a speech parameter that might distinguish mild AD patients from normal individuals. The examination of the temporal parameters of speech in mild AD is of particular interest as it can provide insight into cognitive processes (such as speech planning, structural organization, and production), detect mild changes and track cognitive decline. Spontaneous speech examination is a relatively inexpensive and easy to use technique, and additionally involves minimum discomfort for the patient (Appell, Kertesz, & Fisman, 1982; Kemper, Kemper, Thompson, & Marquis, 2001; Kemper, Marquis, & Thompson, 2001; Kempler, Almor, Tyler, Andersen, & MacDonald, 1998; Kertesz & Munoz, 2003; Schwartz, Federmeier, Van Petten, Salmon, & Kutas, 2003). Speech analysis could be a useful method in examining, even diagnosing mild AD (Illes, 1989).

A number of cognitive tests have been used to differentiate between the various stages of AD, however the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) still remains the most commonly used screening tool (Small, Herlitz, Fratiglioni, Almkvist, & Bäckman, 1997). The MMSE provides a brief

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composite measure of mental status and is the most frequently used index to stratify the severity of dementia (Storey, Kinsella, & Slavin, 2001), despite some inadequacies (Tombaugh & McIntyre, 1992).

Since its initial description (Alzheimer, Forstl, & Levy, 1991), AD has been known to involve language impairment. The lexico-semantic and pragmatic domains of language (Gainotti, 1993; Greene & Hodges, 1996; Huff, Becker, Belle, & Nebes, 1987) are the most affected in AD. For example, patients present with anomia (word-finding difficulty), abnormal verbal fluency (Caramelli, Mansur, & Nitrini, 1998) and difficulty in accessing irregular morphology (Ullman et al., 1997). These results suggest that language impairment in AD involves damage to lexico-semantic representations or difficulty in accessing lexico-semantic representations (Ullman, 2001, 2004). Until reaching the severe stage of AD, the phonological and syntactic domains of language and speech articulation appear to often remain intact (Caramelli, Mansur, & Nitrini, 1998; Cohn, Wilcox, & Lerer, 1991) though there is some evidence for phonological impairments in mild AD (Croot, Hodges, Xuereb, & Patterson, 2000).

Only a handful of studies have examined spontaneous speech in AD (Blanken, Dittmann, Haas, & Wallesch, 1987; Bschor, Kuhl, & Reischies, 2001; Bucks, Singh, Cuerden, & Wilcock, 2000; Forbes, Venneri, & Shanks, 2002; Illes, 1989; Romero & Kurz, 1996; Singh, Singh, Bucks, & Cuerden, 2001), reporting more errors in language production in the patient group than in healthy controls. To date, there has been hardly any investigation of the temporal parameters of spontaneous speech in AD. Investigation of the temporal parameters of spontaneous speech is important because it provides particularly sensitive measures of a subject's speech and language skills (Baum, Blumstein, Naeser, & Palumbo, 1990; Illes, 1989). The present study attempts to fill this gap. We examine temporal parameters of spontaneous speech at different stages of AD with the aim of identifying speech parameters that might distinguish (even mild) AD patients from normal controls and that could potentially indicate the degree of severity of the disease (i.e., mild, moderate, severe).

Method

Participants

A total of 45 participants (30 AD patients and 15 healthy controls) participated in the study (Table I). The patients with AD included 21 females and 9 males. All participants with AD met the DSM-IV and the ICD-10 criteria for probable AD (APA, 1994). Results of neurological, laboratory (including computed tomography (CT) or magnetic resonance (MR) scan), and neuropsychological assessment failed to suggest other causes of dementia. All patients with AD were right-handed, literate, monolingual native speakers of Hungarian and had negative medical history for hearing impairment. They were free of medication at the time of examination. Based on their MMSE scores, the patients with AD were classified into three subgroups. Patients with scores between 21 to 26 were classified as mild AD, patients with scores between 15 and 21 as moderate AD, and patients with scores from 0 to 14 as severe AD (Germano & Kinsella, 2005; Haxby et al., 1988; Perry, Watson, & Hodges, 2000).

The normal control (NC) group included 15 healthy participants (8 females and 7 males) who were right-handed, literate, monolingual native speakers of Hungarian. The NC group did not differ from the AD group in either age ($F(3,41) = .578$, $p = .632$) or years of education ($F(3,41) = .391$, $p = .759$). This study was approved by the Ethics Committee of the University of Szeged. The work was conducted in accordance with the Declaration of Helsinki. The participants and/or their caregivers signed an informed consent form prior to being tested.

Methods

Participants were tested individually by the first author at the Alzheimer Disease Research Centre clinic at the University of Szeged. Following a brief warm-up period (1–2 min), participants were asked (1) to explain why s/he was at the clinic, (2) to recount some important events in their lives and (3) to describe a daily activity or hobby. Sessions lasted between 5 and 8 minutes and were recorded using an Olympus Digital Voice Recorder (WS-311M).

Table I. Participant information.

	MMSE score			Age			Years of education		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
AD mild (n = 10)	25.8	.42	25–26	71	8.5	55–77	11.8	.42	11–12
AD moderate (n = 10)	19.8	1.54	18–21	69.4	9.4	59–82	13.5	5.05	8–20
AD severe (n = 10)	9.4	2.54	5–12	71.4	3.1	66–74	11.2	1.30	8–16
NC (n = 15)	28.6	.42	27–30	67.8	8.5	55–80	12.1	3.70	8–20

Key: NC: normal control, AD: Alzheimer's disease.

A 4-minute speech sample was extracted from each session for analysis (Blanken et al., 1987; Illes, 1989). These samples were written in Hungarian spelling. For each sample, an oscillogram was created using Praat software (http://www.fon.hum.uva.nl/praat/). The following variables were measured in these samples: articulation rate (1), speech tempo (2), hesitation ratio (3), and ratio of grammatical errors (4).

(1) *The articulation rate* (phonemes per second) was calculated as follows. First, from the four-minute speech sample (which consisted exclusively of participants' speech) we eliminated all hesitations (see below for definition of hesitations). We then calculated the total number of phonemes produced by the subject in the remaining time, and divided it by the remaining time.
(2) *The speech tempo* (phonemes per second) was calculated in a similar manner except that hesitations were not eliminated. Thus, we calculated the total number of phonemes produced by the subject during the full 4-minute speech sample and divided it by 4 minutes.
(3) *The hesitation ratio* was calculated as the total duration of hesitations during the 4-min. sample divided by 4 minutes.
(4) *The grammatical error ratio* was calculated as the total number of grammatical errors (i.e. errors in the areas of syntax, inflectional or derivational morphology) divided by the total number of utterances produced by the subject during the 4-minute sample.

A hesitation was defined as absence of (subject) speech during more than 30ms (Gósy, 1998).

The above parameters were compared among the mild, moderate and severe AD groups and normal controls. Statistical analyses involved Kruskal-Wallis, Mann-Whitney and Spearman's correlation tests carried out in SPSS.

Results

Table II provides descriptive statistics for each of the four groups on each of the four speech parameters.

Examination of differences between the four groups (mild AD, moderate AD, severe AD, and NC) on each parameter was carried out by means of the Kruskal-Wallis test, given the non-normal distribution of the data. The effect of group was significant with respect to each of the four parameters (Table III).

To compare the groups pair-wise, we conducted Mann-Whitney tests. We report pair-wise comparisons for each of the parameters in turn.

Articulation rate (Figure 1)

The mild AD group did not differ significantly from the NC group ($U = 49$, $p = 0.16$), but there was a significant difference between the moderate AD and NC ($U = 21$, $p < 0.001$) and between the severe AD and NC group ($U = 22$, $p < 0.001$). Among AD groups, mild AD versus moderate AD ($U = 24$, $p = 0.05$) and mild AD versus severe AD ($U = 24$, $p = 0.05$) differed significantly from each other, but there was no significant difference between moderate AD versus severe AD groups ($U = 42$, $p = 0.58$).

Speech tempo (Figure 1)

The mild AD group significantly differed from the NC group ($U = 26$, $p = .01$): Likewise, the moderate AD and the severe AD groups each differed significantly from the NC group ($U = 2$, $p < .001$ and $U = 4$, $p < .001$, respectively). Among AD groups, the difference between mild AD and moderate AD ($U = 12$, $p < .001$), as well as the difference between mild AD and severe AD ($U = 24$, $p = .05$) were statistically significant, whereas no

Table III. Test statistics (a, b)—examination of differences between the four groups (normal control (NC), mild AD, moderate AD and severe AD) on each parameter.

	Articulation rate	Speech tempo	Hesitation rate	Grammatical error rate
Chi-Square	14.678	27.257	35.420	29.284
df	3	3	3	3
Asymp. Sig.	.002	.000	.000	.000

a Kruskal Wallis Test.
b Grouping Variable: group.
Key: NC: normal control, AD: Alzheimer's disease.

Table II. Speech parameters for AD groups and normal controls (NC).

	Articulation rate (#phonemes/sec)			Speech tempo (#phonemes/sec)			Hesitation ratio (%)			Grammatical errors (%)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
AD mild (n = 10)	10.84	1.52	8.8–12.5	7.76	1.31	6.6–9.9	28.52	6.32	20.4–35.8	5.2	1.22	4–7
AD moderate (n = 10)	9.38	1.7	6.9–11.9	5.34	1.49	3.5–7.5	43.6	8.6	33.1–55.7	6.2	1.23	4–7
AD severe (n = 10)	9.52	1.73	6.9–12.1	5.8	1.95	2.9–7.5	45.44	6.69	38.3–57.1	46	20.46	9–61
NC (n = 15)	11.48	1.08	9.8–13.1	9.5	1.11	7.2–11.1	18.39	4.74	9.8–28	4.33	1.29	3–7

Key: NC: normal control, AD: Alzheimer's disease.

significant difference was observed between moderate AD and severe AD groups (U = 46, p = .80).

Hesitation ratio (Figure 2)

The mild AD group significantly differed from the NC group (U = 16, p < .001). Likewise, the moderate AD and the severe AD groups each differed significantly from the NC group (U = 0, p < .001 and U = 0, p < .001, respectively). Among AD groups, significant differences were observed between mild AD versus moderate AD (U = 4, p < .001), between mild AD and severe AD (U = 0, p < .001), but not between moderate AD and severe AD groups (U = 40, p = .48).

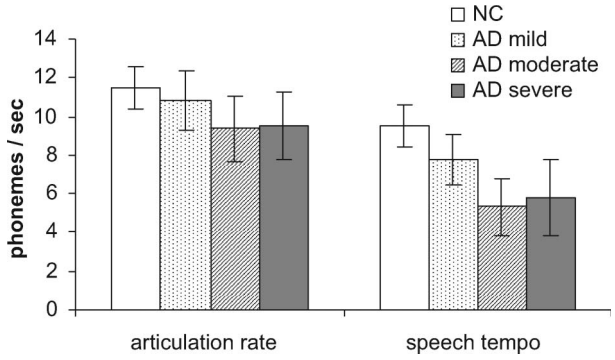

Figure 1. Mean articulation rates and mean speech tempo by subject group (NC: normal control, AD: Alzheimer's disease). *Articulation rate*: the mild AD group did not differ significantly from the NC group, but the moderate AD and the severe AD differed. Among AD groups, mild AD vs. moderate AD and mild AD vs. severe AD differed significantly from each other, but there was no significant difference between moderate AD vs. severe AD groups. *Speech tempo*: all AD groups differed significantly from the NC group. Among AD groups, the difference between mild AD and moderate AD, as well as the difference between mild AD and severe AD were significant, whereas the moderate AD did not differ significantly from the severe AD group.

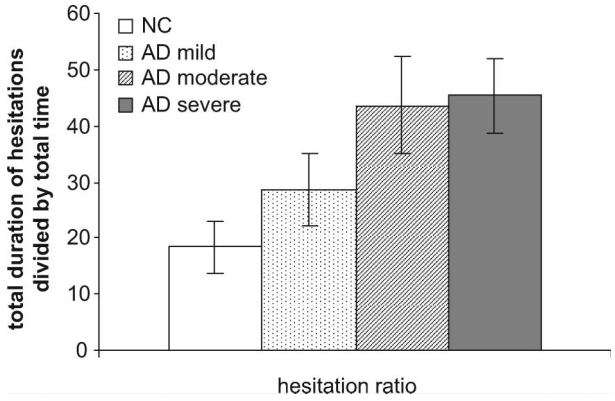

Figure 2. Mean hesitation ratios by subject group (NC: normal control, AD: Alzheimer's disease). All AD groups differed significantly from the NC group. Among AD groups, significant differences were observed between mild AD vs. moderate AD, between mild AD and severe AD, but not between moderate AD and severe AD groups.

Grammatical errors (Figure 3)

Grammatical errors were mainly observed in the severe AD group; the other three groups showed only very low rates. The mild AD group did not significantly differ from the NC group (U = 46, p = .12). Conversely, the moderate AD and the severe AD groups each differed significantly from the NC group (U = 23, p < .001 and U = 0, p < .001, respectively). Among AD groups, significant differences were observed between mild AD and severe AD (U = 0, p < .001), and between moderate AD and severe AD groups (U = 0, p < .001), but not between mild AD versus moderate AD (U = 28, p = .11).

A Spearman's correlation test was performed to test for relations between MMSE scores (considered indicative of the overall disease progression) and the four parameters under investigation as well as between MMSE and the age of the participants. Results revealed a significant positive correlation between the MMSE scores and speech tempo ($\rho = .723$, p < .001), indicating slower tempo for patients with a more advanced form of the disease. A significant negative correlation was observed between MMSE scores and hesitation ratio ($\rho = -.844$, p < .001), and between MMSE scores and grammatical errors ($\rho = -.751$, p < .001), indicating higher hesitation ratio and higher grammatical error ratio for patients with a more advanced from of the disease. There was also a significant correlation between MMSE scores and articulation rate ($\rho = .55$, p < .001), but not between MMSE scores and the age of the participants (Table IV).

Discussion

The purpose of the present study was to investigate temporal parameters of spontaneous speech in AD

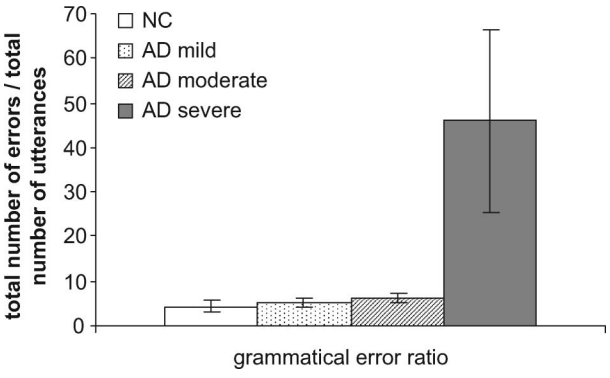

Figure 3. Mean grammatical error ratios by subject group (NC: normal control, AD: Alzheimer's disease). The mild AD group did not significantly differ from the NC group. Conversely, the moderate AD and the severe AD groups each differed significantly from the NC group. Among AD groups, mild AD vs. severe AD and as well as moderate AD vs. severe AD differed significantly from each other, but there was no difference between mild AD vs. moderate AD.

Table IV. Correlation study (Spearman's rho): age, MMSE, articulation ratio, speech tempo, hesitation ratio and grammatical error ratio. All participants (normal controls and patients with Alzheimer's Disease) were included in the analysis.

		Age	MMSE	Speech tempo	Articulation rate	Hesitation ratio	Grammatical error ratio
Age	Correlation Coefficient	1.000	−.159	−.020	.191	.136	.235
	Sig. (2-tailed)	–	.297	.895	.209	.374	.120
	n	45	45	45	45	45	45
MMSE	Correlation Coefficient	−.159	1.000	.723**	.552**	−.844**	−.751**
	Sig. (2-tailed)	.297	–	.000	.000	.000	.000
	n	45	45	45	45	45	45
Speech tempo	Correlation Coefficient	−.020	.723**	1.000	.853**	−.878**	−.526**
	Sig. (2-tailed)	.895	.000	–	.000	.000	.000
	n	45	45	45	45	45	45
Articulation ratio	Correlation Coefficient	.191	.552**	.853**	1.000	−.641**	−.279
	Sig. (2-tailed)	.209	.000	.000	–	.000	.063
	n	45	45	45	45	45	45
Hesitation ratio	Correlation Coefficient	.136	−.844**	−.878**	−.641**	1.000	.722**
	Sig. (2-tailed)	.374	.000	.000	.000	–	.000
	n	45	45	45	45	45	45
Grammatical error ratio	Correlation Coefficient	.235	−.751**	−.526**	−.279	.722**	1.000
	Sig. (2-tailed)	.120	.000	.000	.063	.000	–
	n	45	45	45	45	45	45

**Correlation is significant at the 0.001 level (2-tailed).
Key: MMSE = Mini-Mental State Examination.

and to identify a feature that might distinguish mild patients with AD from normal controls. We found that temporal parameters of speech are indeed affected by AD. Our main finding consists in the discovery of significant differences between the mild AD group and the NC group with regard to speech tempo and hesitation ratio. As illustrated in Figures 1 and 2, the predictive value of hesitation ratio (unlike the other speech parameters) as a screening instrument for the detection of AD is high, as the there is no overlap between the standard deviations for the NC and the mild AD groups on this measure. This feature can also differentiate between the stages (mild and moderate/severe) of AD. Contrary to some previous findings (Singh et al., 2001) there were no significant differences between groups in articulation rate.

The present results might be accounted for by impaired processes of lexical access and word finding difficulties widely documented in AD, which have been reviewed in the Introduction. In naming and TOT (tip of the tongue) tasks patients with AD show significantly worse performance than controls (Abeysinghe, Bayles, & Trosset, 1990; Astell & Harley, 1996; Bayles, 1982; Bayles & Tomoeda, 1983; Cuetos, Martinez, Martinez, Izura, & Ellis, 2003; Cummings, Benson, Hill, & Read, 1985; Kirshner, Webb, & Kelly, 1984; Martin & Fedio, 1983). Lexical decision reaction time studies show longer overall latency in AD than in mild cognitive impairment (MCI) and in normal (elderly) controls (Taler & Jarema, 2006, Cuetos et al., 2003; Walla et al., 2005). In AD the observed longer duration of hesitations in spontaneous speech could be due to decreased lexical access. Increased duration of hesitations may be the first symptom of word finding difficulty in AD.

Future studies need to be conducted in additional types of patient groups (i.e., in other types of dementia) to further test the present findings. To determine whether individual progress of the disease is indeed accompanied by the slowing down of speech tempo and by the increase in the length of hesitations, it is also important to test the present findings in a longitudinal study; such a study is currently under way.

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