Articulatory Agility in Cognitive Decline

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Key Words

Cognitive decline • Articulatory agility • Alzheimer's disease • Motor speech disorders

Abstract

Objective: Motor speech disorders are believed to be uncommon in early Alzheimer's disease (AD). However, data from maximum performance tests of motor speech function in AD and related disorders are virtually nonexistent. The aim of this study was to make such data available. **Materials and Methods:** Sequential speech motion rate was analyzed in 236 memory clinic patients with different levels of cognitive functioning. **Results:** Sequential speech motion rate was moderately but significantly decreased in mild dementia in AD. About 10% of AD and mild cognitive impairment cases had markedly decreased rates. Rates were strongly reduced in progressive nonfluent aphasia, whereas semantic dementia did not differ from subjective cognitive impairment. Frontotemporal dementia had lower rates than AD. **Conclusions:** A proportion of patients with cognitive decline has markedly reduced articulatory agility. The cause of this reduction in some patients with mild cognitive impairment and mild AD is unknown. Semantic dementia is not associated with impaired articulatory agility.

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Introduction

A range of neurodegenerative diseases can cause motor speech disorders. Examples include Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration, spinocerebellar atrophy, and Creutzfeldt-Jakob's disease [1]. In Alzheimer's disease (AD), motor speech disorders are thought to be absent, although one third of the patients eventually develop logoclonia, a speech disorder characterized by rapid and effortless syllable repetitions [2]. In recent years, phonological and articulatory deficits have been described in atypical AD [3]. Such patients have marked motor speech impairments resembling apraxia of speech. However, the prevalence of motor speech disorders in larger samples of cognitive decline including mild AD and the prototypical frontotemporal lobar degeneration syndromes [frontotemporal dementia (FTD), progressive nonfluent aphasia (PNFA), and semantic dementia (SD)] remains unknown.

Apart from vascular subcortical changes, there are three main sites where early Alzheimer-type changes might impede articulatory capacity: the anterior parahippocampal region, the locus coeruleus complex, and the cholinergic forebrain nuclei. At the earliest pathoanatomical stages of AD, neurofibrillary tangles and their precursors accumulate in the anterior parahippocampal

Table 1. Background data for the participants

Diagnosis	n	Sex (male/female)	Age	Education, years	MMSE
Alzheimer's disease	58	27/31	66.03 (8.75)	11.31 (3.62)	23.52 (3.63)
Mild cognitive impairment	89	42/47	61.24 (7.49)	11.98 (3.76)	27.64 (1.98)
Subjective cognitive impairment	60	23/37	57.62 (7.80)	12.73 (2.92)	29.10 (0.98)
Frontotemporal dementia	13	4/9	60.23 (7.07)	13.08 (3.86)	22.58 (4.94)
Progressive nonfluent aphasia	7	2/5	65.00 (4.47)	11.00 (3.52)	22.71 (5.28)
Semantic dementia	9	6/3	60.67 (3.97)	11.89 (3.26)	26.50 (0.55)
Grand mean			61.53	12.04	26.54

Means with standard deviations in parentheses are given for age, education, and Mini-Mental State Examination (MMSE) score.

region, the perirhinal cortex of which receives afferents from several unimodal and polymodal cortical fields, including the insular, medial frontal, and orbitofrontal regions [4]. The parahippocampal region itself projects to prefrontal fields via the efferent trunk of the limbic loop from posterior association fields to the prefrontal fields [5]. The insular and medial frontal regions are both involved in speech production, and degeneration in closely connected areas might affect their functioning by disconnection.

Another early site for Alzheimer-type pathology is the noradrenergic locus coeruleus complex located in the upper pons. This nuclear complex is selectively affected among brainstem nuclei in mild cognitive impairment (MCI) and mild AD [6]. It projects diffusely to the frontal cortex, hippocampal formation, and cerebellum, and receives important afferents from the orbitofrontal and anterior cingulate cortices [7]. Apart from its role in arousal and attention, the locus coeruleus participates in the regulation of motor activity and helps optimizing task performance [7, 8]. Conceivably, therefore, neurofibrillary pathology of the locus coeruleus could affect articulatory capacity.

The cholinergic magnocellular nuclei of the basal forebrain are a third predilection site for Alzheimer-type pathology. The nucleus basalis of Meynert is a cholinergic nuclear complex that is affected very early in AD. This complex has a laterally positioned component called the nucleus subputaminalis of Ayala [9, 10]. It may be specific to *Homo sapiens*, shows bilateral asymmetry (left larger than right), and projects to the posterior part of the inferior frontal gyrus, indicating that it is specialized for speech. Šimić et al. [10] further proposed that this nucle-

us may be involved in progressive aphasia as well as atypical AD, particularly when apraxia of speech prevails.

Because normal speakers are able to adapt their articulatory behavior to adverse conditions [11, 12], it is possible that small yet significant reductions in articulatory agility may be compensated for in casual speech and pass unobserved unless maximum performance tests are used. Unfortunately, quantitative data derived from stringent tests of articulation in AD and related disorders are not available to guide clinical assessment. Such data might be helpful in the differential diagnosis of neurodegenerative disorders in which motor and cognitive deficits often co-occur. To provide preliminary data in these areas, we collected and analyzed maximum sequential speech motion rates in a large case series at a memory clinic. The basic hypothesis was that rates would be impaired in the syndrome characterized by nonfluent speech, that is, PNFA.

Materials and Methods

Subjects

Retrospective clinical data from 236 patients were used in the study. There were 132 women and 104 men. All patients had undergone a standard examination for cognitive impairment at the Memory Clinic, Karolinska University Hospital, Stockholm, Sweden. The clinical examinations included neurological and psychiatric evaluations, neuropsychological assessment, magnetic resonance imaging or computed tomography of the brain, routine blood chemistry, and lumbar puncture with analysis of cerebrospinal fluid. The sequential speech motion rate data were collected as part of a speech-language assessment performed by the first author (P.Ö.). The Mini-Mental State Examination [13] was used to grade the global cognitive state but was not pivotal to the diagnosis.

Participants came from six diagnostic categories:

Dementia in AD. Diagnoses were based on ICD-10 criteria [14]. The dementia was mild on average as indicated by the mean Mini-Mental State Examination score (table 1).

Mild Cognitive Impairment. MCI was diagnosed according to modified Petersen criteria [15]. Thus, MCI participants had subjective memory complaints but also objective signs of decline in any cognitive ability such as memory or visuospatial skill. Objective signs were defined as performance at least 1.5 standard deviation units below age-matched controls on standardized neuropsychological tests. Activities of daily living were intact, and participants did not fulfill the ICD-10 or DSM-IV criteria for dementia.

Subjective Cognitive Impairment. These participants had been referred because of subjective cognitive complaints but were found, after careful assessment, not to fulfill diagnostic criteria for either dementia or MCI but sometimes to feel forgetful in everyday life. By definition, subjective cognitive impairment (SCI) participants thus had no objective cognitive deficits. SCI was therefore adopted as a control group.

Three prototypical clinical syndromes associated with frontotemporal lobar degeneration were diagnosed according to international consensus criteria [16]:

Semantic Dementia. These patients had fluent conversational speech but severely impaired picture naming and deficits in word comprehension. Reading and spelling tasks showed surface alexia and surface agraphia. All cases had asymmetric anterior temporal lobe atrophy on magnetic resonance imaging. One case developed motor neuron disease late in the course.

Frontotemporal Dementia. These patients had marked changes in comportment and insight, with inappropriate and careless conduct. Spontaneous speech was often reduced. Two patients showed signs of motor neuron disease late in the course; a third case had such signs, including mild dysarthria, at the time of assessment.

Progressive Nonfluent Aphasia. PNFA patients had more or less nonfluent, effortful spontaneous speech, often with irregular articulatory breakdowns and stuttering-like repetitions. One case went on to develop signs of motor neuron disease.

Background data for the subjects are given in table 1. Mini-Mental State Examination scores differed between the diagnostic categories [$F(5, 225) = 37.22, p < 0.001$], including significant differences between the three largest participant groups (Bonferroni: SCI vs. MCI, $p < 0.05$; SCI vs. AD, $p < 0.001$; MCI vs. AD, $p < 0.001$).

Speech Motor Task

Sequential speech motion rate was assessed by an experienced speech-language pathologist (P.Ö.) as part of a multidisciplinary dementia examination with a maximum performance test of motor speech function, the widely used 'pataka' test [17]. It requires rapid ordered movement between three places of stop consonant articulation (labial, alveolar, and velar) and devoicing of stop segments. The test is sensitive to motor speech disorders [1], and normative data are available for different groups [17]. Administration was as follows: after a brief demonstration and training session, subjects were instructed to take a deep breath and repeat the non-word syllable sequence [pataka] as quickly and evenly as possible for 10 s. A digital electronic chronograph was used to time the 10 s. Participants were given additional demonstration and train-

ing as needed. The number of correct repetitions was counted. Transposed sequences (e.g. [pakata]) or incomplete sequences (e.g. [paka paka]) were not counted as correct repetitions. Sequential speech motion rate was calculated as the number of correctly repeated [pataka] sequences per second.

Statistical Analysis

The Statistica data analysis software system, version 7.1 (Statsoft, Inc., 2005), was used as the computational tool. The significance level was $\alpha = 0.05$ in all analyses. Analysis of correlation (Pearson's product-moment correlation coefficient) was conducted on age and years of education as potential confounders of diagnostic comparisons. A 2 (sex) $\times$ 6 (diagnosis) ANCOVA with years of education as a covariate was run to explore diagnostic category differences in sequential speech motion rate and to exclude a sex $\times$ diagnosis interaction. Post hoc analysis was conducted with a Bonferroni multiple comparisons test.

Ethical Approval

The study was approved by the Regional Ethics Committee in Stockholm (2007/1469-31/4).

Results

A correlational analysis was first conducted to assess whether sequential speech motion rate was associated with age and education so as to confound diagnostic comparisons. No significant correlations were found between age and sequential speech motion rate ($r = 0.05, p = 0.46$) or between age and education ($r = -0.09, p = 0.18$). However, there was a weak but significant correlation between education and sequential speech motion rate ($r = 0.19, p < 0.01$). Education was therefore included as a covariate in the subsequent analysis. Moreover, the average sequential speech motion rate was significantly higher in male participants than in females (4.79 syllables/s and 4.33 syllables/s, respectively; $t = 2.26, p < 0.05$). To rule out a potential interaction between sex and diagnostic category, both variables were included as independent category variables in an ANCOVA.

The ANCOVA showed a significant main effect of diagnostic category [$F(5, 218) = 14.12, p < 0.001$] as well as a significant effect of the covariate education ($F = 7.52, p < 0.01$). There was no significant main effect of sex ($F < 1, n.s.$) and no significant sex $\times$ diagnostic category interaction ($p = 0.23$). Mean sequential speech motion rates for the six diagnostic categories are presented in table 2. Because the covariate-adjusted means only differed from the observed means in the first or second decimal unit, the adjusted values are not presented.

The specific diagnostic category differences were explored with a Bonferroni multiple comparisons test (ta-

Fig. 1. Frequency scatterplot of sequential speech motion rate (SSMR) across diagnostic categories.

Table 2. Descriptive data for sequential speech motion rate

Group	n	Sequential speech motion rate
Alzheimer's disease	60	5.16 ± 0.97
Mild cognitive impairment	89	4.56 ± 1.46
Subjective cognitive impairment	58	4.31 ± 1.41
Frontotemporal dementia	13	3.40 ± 1.95
Progressive nonfluent aphasia	7	1.07 ± 1.75
Semantic dementia	9	5.83 ± 1.27
Total	236	4.53 ± 1.56

Table 3. Results of Bonferroni multiple comparisons test

Diagnosis	SCI	MCI	AD	SD	FTD	PNFA
SCI	–					
MCI	n.s.	–				
AD	*	n.s.	–			
SD	n.s.	n.s.	*	–		
FTD	***	n.s.	n.s.	***	–	
PNFA	***	***	***	***	**	–

Significant contrasts are indicated by asterisks. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.001$. n.s. = Not significant.

ble 3). Rates were significantly higher in SD than in other categories except SCI and MCI. Conversely, the SCI category had significantly higher rates than other categories except SD and MCI, whereas the PNFA category had significantly lower rates than all other categories.

An examination of the performance within categories by means of a frequency scatterplot showed that 9 cases of MCI (10.1%) and 5 cases of AD (8.6%) had rates below 3.0 syllables/s, that is, 2.2 standard deviation units or more below the SCI mean. By contrast, only 1 SCI participant (1.7%) performed at this level (fig. 1).

Discussion

This study explored a maximum performance test of motor speech function in patients with cognitive decline. Sequential speech motion rate was strongly decreased in PNFA. The very low performance level in this category, significantly worse than the other five diagnoses, probably reflects an apraxia of speech that made patients unable to execute the sequence of alternating articulatory gestures. In contrast, SD had the highest mean sequential speech motion rate in the sample, although not significantly higher than SCI and MCI. FTD showed an inter-

mediate-level performance, significantly better than PNFA but significantly lower than SCI and SD. Apparently, then, sequential speech motion rate can help to distinguish and quantify motor aspects of speech fluency across frontotemporal lobar degeneration syndromes in clinical assessment and research.

Sequential speech motion rate was also significantly lower in AD than in SCI. About 10% of AD and MCI participants performed at an impaired level, with sequential speech motion rates below 3.0 syllables/s. The factors behind these decrements are unclear. In AD, very low performance was seen in some relatively young patients with mild but noticeable apraxia of speech, including hesitations, stuttering-like syllable repetitions, slight vowel distortions, and occasional articulatory groping behavior. Impaired performance among MCI participants was not associated with such signs in spontaneous speech, nor was there any known background of developmental apraxia of speech or other speech-language disorders in the cases with strikingly low performance.

Our data, although limited to group level analyses, may help in deciding what is typical and atypical motor speech performance in patients with syndromes associated with cognitive decline. They complement the detailed observations based on speech samples from ten cases of atypical AD [3]. Such cases have deficits resembling apraxia of speech; on autopsy, they sometimes show AD-type pathology with an atypical anatomical distribution. The presence of apraxia of speech makes it difficult to tell them apart clinically from cases of PNFA with non-Alzheimer pathology. Possibly, articulatory agility is affected by the pathology (or pathologies) behind MCI and mild AD, but not so much as to cause perceptible derangement of speech in most cases. It should be noted that vascular changes in cholinergic pathways may also affect performance in AD patients [18]. Sequential speech motion rate may be a valuable measure of speech produc-

tion in studies that explore the impact of white matter changes on motor and cognitive functions.

A number of limitations to this study should be mentioned. SCI was used as a control group but not recruited as healthy controls. Rather, SCI may be regarded as a group of 'worried well' who went through a comprehensive assessment procedure without fulfilling criteria for any objective cognitive disorder. It cannot be excluded that this category includes some very early cases of progressive cognitive decline that were not detected by the diagnostic methods currently used. Another limitation is the use of a single measure of motor speech function. The sequential speech motion task with its demand for rapid change of place of articulation is perhaps more sensitive to apraxia of speech than to mild forms of dysarthria. Consequently, some cases of incipient dysarthria were perhaps not adequately reflected by this measure. Finally, to count the number of correct repetitions during a 10-second interval is a relatively crude performance measure that does not capture the phonetic detail available from a recording and acoustic-phonetic analysis.

To conclude, this study produced evidence consistent with decreased articulatory agility in a proportion of AD and MCI patients and more marked decrements in PNFA and FTD. Articulatory agility was not affected in SCI and SD. Because the majority of patients with mild AD did not have reduced motor speech performance overall, marked phonological and articulatory deficits are atypical in AD and should prompt a thorough assessment of speech and language.

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References

- 1 Duffy JR: Motor Speech Disorders: Substrates, Differential Diagnosis, and Management. Boston, Mosby, 1995.
- 2 Sjögren T, Sjögren H, Lindgren ÅHG: Morbus Alzheimer and morbus Pick. A genetic, clinical and patho-anatomical study. *Acta Psychiatr Neurol Scand Suppl* 1952;82:1–152.
- 3 Croot K, Hodges JR, Xuereb J, Patterson K: Phonological and articulatory impairment in Alzheimer's disease: a case series. *Brain Lang* 2000;75:277–309.
- 4 Kent RD, Tjaden K: Brain functions underlying speech; in Hardcastle WJ, Laver J (eds): *The Handbook of Phonetic Sciences*. Oxford, Blackwell, 1997, pp 220–255.
- 5 Burwell RD: The parahippocampal region: corticocortical connectivity. *Ann NY Acad Sci* 2000;911:25–42.
- 6 Grudzien A, Shaw P, Weintraub S, Bigio E, Mash DC, Mesulam MM: Locus coeruleus neurofibrillary degeneration in aging, mild cognitive impairment and early Alzheimer's disease. *Neurobiol Aging* 2007;28:327–335.
- 7 Aston-Jones G, Cohen JD: Adaptive gain and the role of the locus coeruleus-norepinephrine system in optimal performance. *J Comp Neurol* 2005;493:99–110.

- 8 Stone EA, Lin Y, Ahsan R, Quartermain D: Role of locus coeruleus α_1 -adrenoceptors in motor activity in rats. *Synapse* 2004;54:164–172.
- 9 Ayala G: A hitherto undifferentiated nucleus in the forebrain (nucleus subputaminalis). *Brain* 1915;37:433–448.
- 10 Šimić G, Mrzljak L, Fučić A, Winblad B, Lovrić H, Kostović I: Nucleus subputaminalis (Ayala): the still disregarded magnocellular component of the basal forebrain may be human specific and connected with the cortical speech area. *Neuroscience* 1999;89:73–89.
- 11 Lindblom B, Lubker J, Gay T: Formant frequencies of some fixed-mandible vowels and a model of speech programming by predictive simulation. *J Phon* 1979;7:147–162.
- 12 Gay T, Lubker J, Lindblom B: Production of bite-block vowels: acoustic equivalence by selective compensation. *J Acoust Soc Am* 1981;69:802–810.
- 13 Folstein MF, Folstein SE, McHugh PR: 'Minimal state.' A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
- 14 World Health Organization: The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research. Geneva, World Health Organization, 1993.
- 15 Wahlund LO, Pihlstrand E, Jönhagen ME: Mild cognitive impairment: experiences from a memory clinic. *Acta Neurol Scand* 2003;107(suppl 179):21–24.
- 16 Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, Freedman M, Kertesz A, Robert PH, Albert M, Boone K, Miller BL, Cummings J, Benson DF: Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology* 1998;51:1546–1554.
- 17 Kent RD, Kent JF, Rosenbek JC: Maximum performance tests of speech production. *J Speech Hear Disord* 1987;52:367–387.
- 18 Behl P, Bocti C, Swartz RH, Gao F, Sahlas DJ, Lancot KL, Streiner DL, Black SE: Strategic subcortical hyperintensities in cholinergic pathways and executive function decline in treated Alzheimer patients. *Arch Neurol* 2007;64:266–272.