Voice quality and speech fluency distinguish individuals with Mild Cognitive Impairment from Healthy Controls

Charalambos Themistocleous,1\* Marie Eckerström,2 and Dimitrios Kokkinakis3,4

1Department of Neurology, Johns Hopkins University, Baltimore, Maryland, United States

2Department of Psychiatry and Neurochemistry, University of Gothenburg, Gothenburg, Sweden

3Department of Swedish, University of Gothenburg, Gothenburg, Sweden

4Center of Ageing and Health - AgeCap, University of Gothenburg, Gothenburg, Sweden

\* Corresponding author:

E-mail: cthemis1@jhu.edu (CT)

# Abstract

Mild Cognitive Impairment (MCI) is a syndrome characterized by cognitive decline greater than expected for an individual's age and education level. This study aims to determine whether voice quality and speech fluency distinguish patients with MCI from healthy individuals to improve diagnosis of individuals with MCI. We analyzed recordings of the Cookie Theft picture description task produced by 26patients with MCI and 29 healthy controls from Sweden and calculated measures of voice quality and speech fluency. The results show that individuals with MCI differ significantly from healthy controls with respect to acoustic aspects of voice quality, namely H1-A3, cepstral peak prominence, center of gravity, and shimmer; and speech fluency, namely articulation rate and averaged speaking time. The method proposed along with the obtainability of connected speech productions can enable quick and easy analysis of speech fluency and voice quality, providing accessible and objective diagnostic markers of patients with MCI.

# Introduction

Mild Cognitive Impairment (MCI) is a syndrome characterized by cognitive decline greater than expected for an individual's age and education level. Individuals with MCI remain functional in their daily activities [1]. Progression rates vary across studies depending on the diagnostic criteria and methods being employed, although there are indications that about 50% of individuals with MCI progress to Alzheimer’s Disease (AD) within five years, yet many patients remain stable for several years [1-3]. Currently, there is no cure for AD, but identifying individuals with MCI early and applying therapy in a timely manner can delay the progression of the MCI to AD [4]. It is of utmost importance, to develop straightforward, not intrusive, and reliable objective diagnostic measurements of cognitive impairment that can be conducted at primary care centers and memory clinics to determine whether an individual should seek further professional advice.

Speech can provide such objective measures for the identification of individuals with MCI. As language impairment is a common symptom of AD, affecting most language domains and functions including phonetics [5, 6], phonology [7], morphosyntactic structure (e.g., mean length of utterances, proportions of nouns and verbs, and syntactic complexity measures), semantics [8, 9], discourse and conversation [7, 10, 11], it can be employed to provide objective diagnostic markers. One of the less understood and studied aspects of language is speech production in individuals with MCI [12, 13]. Speech can convey information about the underlying language system, as it interacts with the other language domains [14-16]. For instance, the slow recall of words can affect speech fluency, especially durational and frequency measures, tonal modulation, and pauses [14-18]. Speech can convey information about motoric and cognitive abilities of individuals with MCI that relate to articulation, voice quality, and fluency. König, Satt (12) employed automated acoustic measures and classified individuals with MCI and healthy controls with 79% classification accuracy, individuals with MCI and AD with 80% accuracy, and individuals with AD from healthy controls with 89% classification accuracy. In our previous work [19], we analyzed segmental and prosodic features of speech production. Namely, we showed that vowel formants (F1 to F5), the fundamental frequency, and vowel duration can distinguish individuals with MCI from healthy controls with 83% mean cross-validated accuracy.

This study aims to identify a few selected features from voice quality and speech fluency that can function as objective markers distinguishing individuals with MCI from healthy controls. An advantage of this study over other studies of language in MCI is that our approach does not require preprocessing, such as transcription and segmentation of the acoustic signal into vowels and consonants. Specifically, we tested two main questions: i. Does voice quality (as estimated by differences between speech harmonics and amplitudes, the cepstral peak prominence (CPP), mean energy concentration of spectral or first spectral moment, the Hammarberg index, jittering, and shimmer) distinguish individuals with MCI from healthy individuals? And ii. Do measures of speech fluency (namely, the averaged speaking time, articulation rate, and speech rate) distinguish individuals with MCI from healthy individuals? To answer these questions, we analyzed acoustically speech productions from the Cookie Theft picture description task from the Boston Diagnostic Aphasia Examination (BDAE) produced by Swedish individuals with MCI and healthy controls [20]. This study shows that voice quality and speech fluency provide information that can identify individuals with MCI from healthy controls.

# Patients and methods

## Participants

The 55 participants were recruited as part of the Gothenburg MCI study, which is a large clinically based longitudinal study on MCI [21]. Details about the participants are provided in Table 1. The Gothenburg MCI study provides an in-depth phenotyping of patients with different forms and degrees of cognitive impairment using imaging/physiologic methods, psychometrics, and biochemical methods, namely Cerebrospinal fluid characterization of substances in the brain. Participants were selected based on specific inclusion and exclusion criteria: (i) no dyslexia and other reading deficiencies; (ii) no current history of major depression, and recent substance abuse; (iii) no history of serious psychiatric, neurological and other brain-related conditions; (iv) to be native Swedish speakers; (v) to be able to read and understand information about the study; and (vi) to be able to provide written consent. Healthy controls had a significantly higher Mini-Mental State Exam score (*M*=29.6). (The MMSE score is a scale of 0–30 and represents the cognitive status of an individual). Mean MMSE score for the MCI participants was 28.2, which is close to normal [22-24]. Ethic approvals, the consent procedure, and data acquisition were approved by the Swedish Ethical Review Authority, <<http://www.epn.se/>> (ref. nr: 206-16, 2016) and the ethics amendment was approved by the same institution (ref. nr: T021-18, 2018). Also, all procedures performed involving human contributors were in accordance with the latest Declaration of Helsinki revision, 2013. Subjects were prospectively recruited from one center: the Memory Clinic at the Sahlgrenska University Hospital, Sweden. All patients provided written informed consent for use of data before the data collection.

TABLE 1 HERE

## Procedure and acoustic measurements

The picture description task was part of additional assessment tests conducted as part of “Linguistic and extra-linguistic parameters for early detection of cognitive impairment” research project funded by Riksbankens Jubileumsfond – The Swedish Foundation for Humanities & Social Sciences (NHS 14-1761:1). This picture shows two children trying to remove cookies from a jar placed on top of a cupboard as their mother is washing the dishes. A clinician presented the picture to participants and prompted them to tell everything they see on the picture following the standard BDAE-3 instructions. The picture description task was audio recorded using a Zoom H4N audio recorder, located at a fixed distance (1ft) in front of the participants. The audio was converted to 16000 Hz mono format [19, 25].

The recordings were analyzed acoustically. Specifically, we analyzed speech sounds and measured acoustic properties related to voice quality and speech fluency. Measurements of voice quality and syllable structure were calculated.

**C1. Voice quality / phonation.** Phonation and voice quality account for the fine control of the sublaryngeal and laryngeal systems. To determine the phonation and voice quality differences of individuals with MCI and healthy controls, we have calculated the following measurements.

1. *H1-H2, H1-A1, H1-A3:* Difference between the first and second harmonics (H1-H2), the first harmonic and first amplitude (H1-A1), and first harmonic and third amplitude (H1-A3) demarcate voice quality. Harmonics are estimated by considering the fundamental frequency, and amplitudes from the spectra. Relative amplitude of first two harmonics H1 and H2 indicates breathy (strong H1) and creaky voice (weaker H2) [26].
2. *Cepstral Peak Prominence (CPP).* CPP is a reliable measure of dysphonia [27]. It accounts for the periodicity in the voice signal: higher values of CCP correspond to greater periodicity. It stands as the relative amplitude of the cepstral peak prominence in relation to the expected amplitude as derived via linear regression.
3. *Mean Energy Concentration* or *first spectral moment* is the average spectral frequency [28, 29].
4. *Hammarberg Index.* The Hammarberg index is the difference between the maximum energy in the 0…2kHz energy band and the energy in the 2…5kHz band. The Hammarberg index is considered an indicator of articulatory effort [30].

Finally, we provide measures of shimmering, jittering, and harmonicity.

1. Jitter (Hz) is the cycle-to-cycle variation of the *fundamental frequency* () (1), expressed as:

where are the extracted period lengths and is the number of extracted periods. The is the basic frequency produced during the vibration of the vocal folds and it is one of the primary acoustic correlates of intonation, which manifests linguistic (e.g., different melodic patterns for questions, and statements) and extralinguistic functions (e.g., emotional prosody) [31]. Reduced control on vocal-fold vibration results in higher percentage of jitter [32].

1. Shimmer (dB) is the variability of the amplitude from peak-to-peak (local maxima). Equation (2) shows shimmer as the mean absolute base-10 logarithm (multiplied by 20) of the difference between the amplitudes of successive periods (2):

where are the extracted peak-to-peak measurements of amplitute and is the number of periods. Shimmer indicates noisy productions and breathiness and it is a correlate of glottal resistance and mass lesions on the vocal folds [32].

**C2. Speech Fluency.** *Speech rate and articulation rate.* These are measures of fluency as described in the introduction. We calculated the following measures: average syllable duration, the articulation rate, and speech rate.

1. *Average Syllable Duration:* Is the mean syllable duration estimated as a measure of the overall speaking time divided by the number of syllables (3).

1. *Articulation Rate:* Articulation rate considers phonation time, which is a measure of phonation times, pauses and silences are thus excluded (4).
2. *Speech Rate*: Is a measure of the number of syllables divided by the overall duration, which includes pauses and silences (5):

For the statistical analysis, we employed linear mixed effects models using condition (MCI vs. HC) and gender as fixed factors on voice quality and phonation measurements (dependent variables) and condition on speech fluency measurements dependent variables. We included gender in the statistics of voice quality and phonation, as they depend on physiological differences between men and women, e.g., lower pitch in men than in women. All acoustic analyses were performed using Praat [33]. The R package emmeans was employed to obtain estimated marginal means (EMMs, also known as least-squares means) for factor combinations in the linear mixed effects models and compute the contrasts or linear combinations of these marginal means.

# Results

**C1. Voice quality / phonation.**

Voice quality measures demonstrate starting changes of individuals with MCI from healthy controls as shown in Fig 1. MCI individuals produce speech that differs from healthy controls in phonation and voice quality, which is measured using objective markers presented in this section and determine differences in the fine-control of the sublaryngeal and laryngeal systems. We found significant differences of individuals with MCI from healthy controls with respect to the difference of the first harmonic and third amplitude (H1-A3), shown in Table 2. Patients with MCI differed significantly from healthy controls with respect to their CPP (see Fig. 2, Panel B). There is an overall lower CPP in individuals with MCI compared to healthy controls, suggesting weaker voice. Also, individuals with MCI differed significantly from HC with respect to shimmer and center of gravity. However, individuals with MCI and healthy controls did not differ significantly with respect to the Hammarberg Index measurement (*F*(1:278)= 0.137, *p* = 0.711). Also, there were no significant differences between individuals with MCI and healthy controls in jitter (*F*(1, 254)= 2.73*, p* = 0.1).



**Fig 1** **Voice quality and phonation elicited from audio recordings produced by individuals with MCI and HC.**

(A)H1-A3 (dB); (B) Cepstral Peak Prominence (dB); (C) Center of Gravity (Hz); and (D) Shimmer (dB) in healthy individuals and individuals with MCI; ‘.’ indicates p < 0.1; ‘\*’ indicates p < .05; ‘\*\*’ indicates p < .01.

TABLE 2 HERE

**C2. Speech Fluency**

Individuals with MCI produced significantly longer syllables from HC, as measured by the average syllable duration and had a slower articulation rate and speech rate but only with respect to average syllable duration and articulation rate we found significant effects (see Fig 2 and Table 3). 

**Fig 2.** **Measures of speech fluency elicited from audio recordings produced by individuals with MCI and HC.**

(A) averaged speaking time; (B) articulation rate; and (C) speech rate in healthy individuals and individuals with MCI; ‘.’ indicates p < 0.1; ‘\*’ indicates p < .05; ‘\*\*’ indicates p < .01.

TABLE 3 HERE

Table 4 presents a summary of the main findings with the acoustic measures that differentiate individuals with MCI from HCs.

TABLE 4 HERE

# Discussion

Cognitive decline in individuals with Mild Cognitive Impairment (MCI) is manifested as a noticeable memory difficulty in remembering events and situations, impaired language, speech, decision making, planning, interpreting instructions, and orientation [1, 21, 34-40]. Given that MCI individuals are a high risk group for developing AD, there is a dire need to elicit objective measures that can enable the early and quick identification of individuals with MCI, to provide treatment promptly, facilitate MCI prognosis, and ultimately improve life quality both for individuals with MCI and for their family members. This study provides novel findings that show impairment of speech production in individuals with MCI with respect to (i) voice quality and (ii) speech fluency and demonstrates that these measures can provide objective diagnostics of individuals with MCI.

*4.1. Voice quality measures of MCI*

An unexpected finding is that individuals with MCI differed from healthy controls with respect to voice quality. Early cognitive impairment is manifested by disparities in voice breathiness and increased dysphonia. Individuals with MCI differed from healthy individuals in H1-A3, which suggests that voice breathiness is different in MCI individuals with respect to healthy controls. Our study shows an increased H1-A3 in individuals with MCI with respect to healthy controls. Tanaka, Adachi (41) report a similar finding in patients with AD vs. healthy controls. A novel finding was that individuals with MCI show lower periodicity in spectra than healthy individuals, which corresponds to greater dysphonia, as measured with the CPP. Individuals with MCI are characterized by overall lower center of gravity; which can correspond to lower frequency speech productions, that result into a significantly weaker speech than healthy individuals of the same age. It also indicates an overall relaxation of articulators during speech production that is manifested by the lowering of the spectral center of gravity. Individuals with MCI are characterized by greater shimmer in speech production which indicates greater instability of amplitude. Greater shimmer may indicate less stability and control of the sublaryngeal/pulmonary pressure. Another important finding is that individuals with MCI are characterized by differences in breathy voice, greater dysphonia, lower center of gravity and shimmer. These findings may be the result of cognitive and physiological impairment of the fine control and the slowing down of the vocal folds, of pulmonary pressure, respiration, and the co-ordination of phonation with articulatory production [15, 42-45].

*4.2. Speech fluency measures*

Individuals with MCI have different speech fluency measures. Our findings show that the overall articulation rate and speech rate are significantly slower in individuals with MCI than in elderly healthy individuals. The slower articulation can be the result of slower cognitive processes due to MCI, affecting attention, memory, and language, including word recall and grammar [1-3]. It can also be the result of impaired motor control as individuals with MCI are characterized largely by abnormalities in motor coordination and disinhibition [46], motor preparation [47], and motor planning [48], which can influence motoric functions related to articulation.

*4.3. Diagnostic utility of speech features*

This study brought together speech acoustics and statistical analysis for the study of speech production in MCI. Speech reveals multidimensional information about the speaker (e.g., age, gender, sociolinguistic characteristics, physiological condition) and can function as a fingerprint that identifies individuals with MCI from healthy controls. The findings provide objective measures from voice quality that distinguish individuals with MCI and healthy individuals and at the same time they point to the importance of phonation and speech fluency as a diagnostic measurements [42-45]. Implemented aa computer application, this approach can provide an easy and accessible interface for the automatic quantification of voice quality and speech fluency, utilized by physicians, neuropsychologists, and speech therapists to quantify speech in tasks, such as picture description tasks, scripts, and discourse. By increasing the span of acoustic measurements that can be analyzed and understanding their corresponding speech deficits [49, 50], physicians, neuropsychologists, and speech therapists can tailor therapeutic programs to the specific needs of their clients (e.g., focusing on targeted part of speech productions). Measures of voice quality and fluency from connected speech, discourse, etc. can enable clinicians to assess the overall speech production of individuals with MCI and provide information about the differential speech properties of patients with MCI variants and healthy controls and ultimately enable a better understanding of speech symptoms of individuals with MCI.

*4.4. Limitations and future directions*

Picture description tasks (e.g., Cookie Theft) constrain the production of speech in that the productions are often narrowed down to labelling rather than on free narration which to a certain degree may constrain fluency measurements. In contrast, storytelling, discourse, and conversation are characterized by expressive variations of fluency. This aspect of fluency cannot be tested using picture description tasks. Future research is important to employ computational analysis of voice quality and speech fluency in free style conversations and in other conditions affecting language, such as stroke aphasia and primary progressive aphasia [e.g., 50, 51, 52-56]. The acoustic measures proposed in this study along with the obtainability of connected speech productions and the availability of acoustic analysis software can enable the rapid analysis of speech in the primary care centers and memory clinics providing accessible diagnostic methods for MCI. Another limitation is the relatively small sample size; a larger sample size is expected to increase the effect size of the model. Also, as speakers are recruited at a single recruitment center, there are may be constrained to the people that participate and represent the overall population. These two limitation will be addressed in our future research as currently we are collecting data from a larger population of patients attending different recruitment centers.

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**Table 1. Demographic information and scores for Memory & Learning, Language, Attention, and Executive function, by group (mean and standard deviation).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | HC (n = 29) | MCI (n = 26) | Sig. |
| Demographic | Age (years) | 67.8 (7.7) | 70.6 (5.8) | \* |
|  | Education (years) | 13.3 (3.7) | 14.3 (3.6) | n.s. |
|  | Sex (F/M) | 21/8 | 14/12 | n.s. |
|  | MMSE (/30) | 29.6 (0.6) | 28.2 (1.4) | \*\*\* |
| Memory/Learning | RAVLT (total) | 45.5 (11.1) | 37.6 (10.7) | \* |
|  | RAVLT (delayed) | 9.2 (3.6) | 5.8 (3.5) | \*\*\* |
|  | RAVLT (immediate) | 9.5 (3.5) | 6.1 (3.1) | \*\*\* |
|  | RCF (3 min) | 18.8 (5.1) | 15.8 (6.8) | n.s. |
|  | RCF (20 min) | 18.6 (4.4) | 14.3 (7.0) | \* |
|  | WLM (delayed) | 21.9 (8.1) | 16.0 (10.5) | \* |
|  | WLM (immediate) | 25.8 (6.3) | 21.3 (7.6) | \* |
| Language | BNT | 53.3 (4.6) | 50.2 (7.6) | n.s. |
|  | Verbal Fluency (F-A-S) | 47.2 (11.5) | 43.6 (11.1) | n.s. |
|  | Similarities | 24.6 (4.7) | 24.0 (5.2) | n.s. |
|  | Token Test (Part 5) | 20.9 (1.4) | 20.0 (1.8) | n.s. |
| Attention | Digit Span | 13.1 (3.5) | 12.4 (2.8) | n.s. |
|  | Digit-Symbol | 62.9 (12.3) | 54.2 (10.8) | \*\* |
|  | TMT A | 34.1 (11.9) | 39.5 (13.3) | n.s. |
|  | TMT B | 79.8 (32.9) | 97.8 (49.4) | n.s. |
|  | Block design | 40.6 (9.5) | 35.5 (12.2) | n.s. |
|  | RCF (copy) | 33.6 (2.4) | 32.4 (3.4) | n.s. |
|  | Silhouettes | 22.4 (4.2) | 19.3 (3.3) | \*\*\* |
| Executive Function | Letter-Digit | 9.5 (2.3) | 8.7 (2.6) | n.s. |
|  | PaSMO | 68.2 (21.5) | 86.8 (29.1) | \* |
|  | Stroop (trial 1) | 13.2(2.4) | 14.6 (3.1) | n.s. |
|  | Stroop (trial 2) | 17.6(3.4) | 19.4 (5.4) | n.s. |
|  | Stroop (trial 3) | 24.1(6.6) | 27.6 (6.6) | \* |
|  | Stroop Effect | 1.8(0.4) | 1.9 (0.5) | n.s. |

RAVLT Rey Auditory Verbal Learning Test; RFC Rey complex figure (RCF); WLM: Word List Memory; BNT Boston Naming Test; TMT A, TMT B Trail Making Test A and B; PaSMO Parallel Serial Mental Operation; ‘\*’ p < .05; ‘\*\*’ p < .01; ‘\*\*\*’ p < .001.

**Table 2. Regression results for the effect of Condition (MCI vs. HC) and gender on H1-A3.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Predictor | *b* | *b*  95% CI  [LL, UL] | *sr2* | *sr2*  95% CI  [LL, UL] | Fit |
| *H1-A3* | Intercept | 26.87\*\* | [25.14, 28.59] |  |  | *R2*  = .137\*\* |
|  | MCI | 2.91\* | [0.52, 5.29] | .02 | [-.01, .05] | 95% CI[.06,.21] |
|  | Male | 9.75\*\* | [6.11, 13.39] | .09 | [.03, .15] |  |
|  | MCI:Male | -5.52\* | [-10.06, -0.97] | .02 | [-.01, .05] |  |
| CPP | Intercept | 71.12\*\* | [70.59, 71.66] |  |  | *R2*  = .057\*\* |
|  | MCI | -1.18\*\* | [-1.92, -0.44] | .03 | [-.01, .07] | 95% CI[.01,.11] |
|  | Male | -1.96\*\* | [-3.08, -0.83] | .04 | [-.00, .08] |  |
|  | MCI:Male | 2.05\*\* | [0.64, 3.46] | .03 | [-.01, .07] | Center of Gravity |
| Center of Gravity | Intercept | 676.96\*\* | [513.71, 840.22] |  |  | *R2*  = .020\* |
|  | MCI | -260.32\* | [-476.29, -44.35] | .02 | [.00, .06] | 95% CI[.00,.06] |
| Shimmer | Intercept | 0.12\*\* | [0.11, 0.13] |  |  | *R2*  = .019\* |
|  | MCI | 0.01\* | [0.00, 0.02] | .02 | [.00, .06] | 95% CI[.00,.06] |

*b* unstandardized regression weights, a significant *b*-weight indicates the semi-partial correlation is also significant. ;*sr2* semi-partial correlation squared; *LL* and *UL* lower and upper limits of a confidence interval; \* *p* < .05; \*\* *p* < .01.

**Table 3. Regression results for the effect of Condition (MCI vs. HC) onaveraged syllable duration, articulation rate, and speech rate*.***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Predictor | *b* | *b*  95% CI[LL, UL] | *sr2* | *sr2*  95% CI[LL, UL] | Fit |
| Average Syllable Duration | Intercept | 38.28\*\* | [32.86, 43.71] |  |  | *R2*  = .063\*\* |
|  | MCI | 11.38\*\* | [3.19, 19.57] | .06 | [.00, .16] | 95% CI[.00,.16] |
| A*rticulation Rate* | Intercept | 65.47\*\* | [58.46, 72.48] |  |  | *R2*  = .060\*\* |
|  | MCI | -14.29\*\* | [-24.87, -3.71] | .06 | [.00, .16] | 95% CI[.00,.16] |
| *Speech Rate* | Intercept | 60.70\*\* | [53.32, 68.08] |  |  |  |
|  | MCI | -10.70 | [-21.85, 0.44] | .03 | [.00, .12] |  |
|  |  |  |  |  |  | *R2*  = .031 |
|  |  |  |  |  |  | 95%CI[.00,.12] |

*b* unstandardized regression weights, a significant *b*-weight indicates the semi-partial correlation is also significant; *sr2* semi-partial correlation squared; *LL* and *UL* lower and upper limits of a confidence interval; ‘\*’ *p* < .05; ‘\*\*’ *p* < .01.

**Table 4. Summary of the main findings.**

|  |  |  |
| --- | --- | --- |
|  | Measure | Result |
| Voice Quality | H1-A3 | Significant differences between patients with MCI vs HC |
| Cepstral Peak Prominence | Significant differences between patients with MCI vs HC |
| Center of Gravity | Significant differences between patients with MCI vs HC |
| Shimmer | Significant differences between patients with MCI vs HC |
| Articulation Rate | Average Syllable Duration | Significant differences between patients with MCI vs HC |
| Articulation Rate | Significant differences between patients with MCI vs HC |
| Speech Rate | Marginal differences (p < 0.1). |