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Changes in Speech Range Profile Are Associated with Cognitive Impairment

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ABSTRACT

Background and Purpose: The aim of this study was to describe the variations in the speech range profile (SRP) of patients affected by cognitive decline.
Methods: We collected the data of patients managed for suspected voice and speech disorders, and suspected cognitive impairment. Patients underwent an Ear Nose and Throat evaluation and Mini-Mental State Examination (MMSE). To obtain SRP, we asked the patients to read 18 sentences twice, at their most comfortable pitch and loudness as they would do in daily conversation, and recorded their voice on to computer software.
Results: The study included 61 patients. The relationship between the MMSE score and SRP parameters was established. Increased severity of the MMSE score resulted in a statistically significant reduction in the average values of the semitones to the phonetogram, and the medium and maximum sound pressure levels (p<0.001). The maximum predictivity of MMSE was based on the highly significant values of semitones (p<0.001) and the maximum sound pressure levels (p=0.010).
Conclusions: The differences in SRP between the various groups were analyzed. Specifically, the SRP value decreased with increasing severity of cognitive decline. SRP was useful in highlighting the relationship between all cognitive declines tested and speech.

Keywords: Speech; Cognitive Impairment; Dementia; Language; Mental Status and Dementia Tests

INTRODUCTION

Measurable changes in cognition occur with normal aging. The most important changes are decline in cognitive tasks that require rapid processing or translation of information to reach a decision, including the speed of processing, working memory, and executive cognitive function.[1,2]

Alarmingly, these changes can be a marker of Alzheimer's disease (AD) or dementia[3] as well as mild cognitive impairment (MCI), which is a common condition in the elderly population.[3] The prevalence of MCI is nearly 4-fold greater than dementia and represents a transitional phase between normal brain status and dementia.[4,5]

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A rapid increase in the global aging population increases the number of patients affected by cognitive decline. The brain in patients with cognitive decline is damaged by an increase in cellular senescence of neurons and microglia, including an increase in apoptosis, aggregation of proteins involved in the formation of amyloid fibrils, mitochondrial dysfunction along with increased reactive oxygen species and oxidative damage to proteins and lipids resulting in the accumulation of damaged DNA.[6] In addition, aging is associated with a decrease in neuronal glucose transporters, resulting in a decrease in glucose uptake by the neurons, and thus a decline in cognitive function.[7]

Livingston et al.[8] in 2020 showed that the age-specific incidence of dementia has declined in many countries, probably because of improved education, nutrition, health care, and lifestyle changes. However, the number of people suffering from dementia is rising. Our understanding of dementia and its etiology has improved with advances in pathology.[8] Newer diagnostic approaches to dementia are being developed using blood biomarkers that are more scalable than cerebrospinal fluid and brain imaging markers.[8] Besides, recent endoscopic or videofluoroscopic studies of swallowing may potentially reveal undiagnosed cognitive impairment.[2,9] Meilan et al reported in a 2018 study that all the tasks used to assess lexical access for oral reproduction of a word were noticeably impaired in patients with AD.[10]

Language and speech disorders such as slurred speech or difficulties in understanding spoken and written language are common in vascular dementia (VD). Progressive non-fluent aphasia mainly affects speech synthesis, whereas semantic dementia is associated with impaired word comprehension and semantic memory. Subclinical signs are apparent in patients with fronto temporal dementia (FTD).[11,12]

Speech is affected by cognitive impairment due to the involvement of Broca's area in the frontal lobe of the dominant hemisphere. This area is linked to speech production and the Wernicke's area in the temporal lobe is involved in the comprehension of written and spoken language. Both these areas are damaged in all types of dementia or cognitive impairment.[12-14]

Curretly, due to the aforemention reasons as well as the recent discovery of a link between oropharyngeal dysphagia, hearing loss, vestibular dysfunction and dementia or MCI[2,15,16] a patient with undiagnosed cognitive decline is most likely to visit an otolaryngologist for initial specialist attention. In this study, we investigated whether a short, non-invasive, inexpensive and simple but precise technique such as the analysis of speech range profile (SRP) could be predictive of cognitive decline to facilitate early diagnosis.

METHODS

This was a retrospective observational study of patients managed for suspected voice and/or speech disorders and suspected cognitive impairment in a tertiary referral centre for voice and speech diseases (U.O. Foniatria, Dipartimento di Riabilitazione, ASL Lecce, Italy). The study spanned 6 months from June 1st, 2020 to December 31st, 2020.

Participants

The exclusion criteria were: patients with clinical history of surgery, chemotherapy or radiotherapy of head and neck region, poor oral health condition, facial nerve paralysis, pharyngolaryngeal diseases such as vocal fold paralysis, gastro-oesophagal pathologies,

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neuromuscular diseases, stroke, inability to perform basic activities of daily living, severe respiratory system disorders that impair normal speech, serious eye diseases or hearing loss making it impossible to read sentences or understand simple orders and patients with psychiatric conditions.

The study included only 61 out of 180 patients consulting for suspected speech or voice disorders and suspected cognitive impairment from June 2020 to December 2020 after screening for the aforementioned exclusion criteria.

All of the patients underwent a detailed Ear Nose and Throat (ENT) evaluation based on their clinical history followed by oropharyngoscopy. Also, patients' oral function was evaluated including assessment of mouth opening, motility of the tongue, soft palate elevation, pharyngeal reflex, voluntary cough and cough reflex, salivation, and dental status. The ENT evaluation was completed with an endoscopic evaluation of pharynx and larynx in all patients.

Speech range profile and Mini-Mental State Examination (MMSE)

To obtain SRPs, we recorded the speaking voice through a XION® headset microphone positioned at 30 cm from the mouth. The voice was analyzed with a DiVAS Voice Diagnostics System by XION®. We asked the patients to read 18 sentences twice, at their most comfortable pitch and loudness as they would do in daily conversation. The sentences were selected based on different prosodic features such as interrogative, affirmative or exclamatory elements as well as expression of different feelings such as happiness, sadness, disbelief and disappointment. The sentences used and indicated in **Table 1** were suitable for any level of patient literacy based on the previous SRP study published by D'Alatri in 2014.[17] The oral reading ability was determined by the Battery for the Analysis of Aphasic Deficits test.[18]

The room where the patients' voices were recorded was noise-free. The SRP was followed by analysis of several parameters, which included the number of semitones, the basic unit of measurement on phonetogram indicated by half tone on the digital keyboard, the sound

Table 1. The selected sentence used

Italian	English
1. Dove stai andando?	1. Where are you going?
2. Attento!	2. Watch out!
3. È abbastanza! Sono stufo delle tue scuse	3. It's enough! I'm sick of your apology
4. Cosa fai nel tuo tempo libero?	4. What do you do in your spare time?
5. Vuoi uscire oggi o domani?	5. Do you want to go out today or tomorrow?
6. Da quanto tempo non visiti Milano?	6. How long have you not visited Milan?
7. Vieni qui!	7. Come here!
8. Sei stanco?	8. You are tired?
9. In che città vivi?	9. In which city do you live?
10. Non essere sciocco!	10. Do not be silly!
11. Sei stato interrogato oggi?	11. Have you been questioned today?
12. Hanno bussato alla porta	12. They knocked on the door
13. A che ora esci di casa?	13. What time do you leave the house?
14. Di che colore è la macchina di papà?	14. What color is dad's car?
15. Non fare tardi!	15. Do not be late!
16. Si prega di seguire attentamente le spiegazioni!	16. Please follow the explanations carefully!
17. Che bella sorpresa!	17. What a nice surprise!
18. Sei felice?	18. Are you happy?

The selected sentences were characterized by different prosodic features such as interrogative, affirmative or exclamatory elements, and express different feelings such as happiness, sadness, disbelief, and disappointment. The sentences are very simple and appropriate for any level of patient literacy.
The English translation of the sentences read is shown alongside the Italian expressions.

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pressure level maximum (SPL max), the sound pressure level medium (SPL med), which represent the pressure level of the sound, measured in decibels (dB) and the speech time (SPT), i.e., the total SPT from first to last syllable produced. Overtones and vocal fry as well single and isolated registrations or small groups of registration disconnected from the principal speech area were omitted in accordance with the previous study of Hallin.[19] Finally, according to our departmental procedures, all included patients were evaluated by a psychologist via MMSE and a score of 24 is the accepted cut-off indicating cognitive decline.[20] Specifically, MMSE values >24 were considered normal, while those between 21 and 24 were considered MCI, values between 10 and 20 were indicative of moderate cognitive decline, and <10 represented severe decline cognitive.[20]

The emergence from clinical and radiological history of multiple cognitive deficits associated with memory decline and one or more cognitive disturbances like aphasia, apraxia, agnosia, impairment in executive functions or social and occupational functions were linked to AD, while decline in memory functions with evidence of clinical or radiological sufference of vascular cerebral circle were associated with VD. Changes in personality, progressive language modification, impaired and progressive decline in occupational and social ability warranted differential diagnosis of FTD. Independence in functional abilities and lack of significant impairment in social or occupational functioning together with light cognitive impairment prompted differential diagnosisis of MCI.

However a neurological evaluation was indicated when the MMSE showed a positive value for cognitive impairment.

Statistical analysis

Quantitative variables were expressed as mean±standard deviation (SD) and categorical variables were reported as frequencies and percentages. The χ^2 test was used to compare proportional values. Independent sample *t*-test and 1-way analyses of variance were performed to explore the differences between SRP parameters, diagnosis, MMSE score and sample characteristics. *Post hoc* analysis was conducted to explore the differences between groups, following one-way analyses of variance. The regression coefficient (+standard error) was calculated to estimate the relationship between SRP parameters, age and years of education. The association between MMSE and SRP parameters analyzed was assessed via multiple linear regression analysis assuming MMSE as a dependent variable and SRP parameters as independent variables. We set the statistical significance at a *p*-value <0.05. All statistical analyses were performed with IBM® SPSS Statistics v 20.0 software (SPSS Inc, Chicago, IL, USA).

This study followed all of the ethical guidelines and rules of our ward.

RESULTS

Males constituted 52.5% of patients and the average age was 71.6 years (±13.1). The general and clinical characteristics of the sample are shown in **Table 2**, including the distribution of variables stratified by gender, education and age, which did not show any statistically significant differences with clinical parameters.

Fourteen patients were found to be healthy and served as the control group in this study. Of the 14 subjects diagnosed with impaired verbal reading skills, 50% were patients with AD,

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Table 2. General and clinical characteristics of sample stratified by sex, years of education and age

Characteristics	Total sample	Sex		*p*-value	Education years	*p*-value	Age (years)	*p*-value
		Male	Female					
Total sample	61 (100.0)	32 (52.5)	29 (47.5)		12.2±4.7		71.6±13.1	
Diagnosis				0.859		0.309		0.100
AD	18 (29.5)	8 (44.4)	10 (55.6)		12.2±5.5		78.5±9.9	
VD	11 (18.0)	6 (54.5)	5 (45.6)		9.8±3.9		66.6±20.7	
FTD	6 (9.8)	3 (50.0)	3 (50.0)		12.8±4.5		71.0±13.2	
MCI	12 (19.7)	6 (50.0)	6 (50.0)		12.1±4.7		70.0±6.7	
Healthy	14 (23.0)	9 (64.3)	5 (35.7)		14.0±4.2		68.4±11.2	
Impairment in oral reading*,†				0.153		0.488		0.065
No	47 (77.0)	27 (57.4)	20 (42.6)		12.4±4.7		69.6±12.4	
Yes	14 (23.0)	5 (35.8)	9 (64.2)		11.4±4.9		78.5±13.2	
MMSE				0.543		0.324		0.758
Normal	14 (23.0)	9 (64.3)	5 (35.7)		14.0±4.2		68.4±11.2	
Mild	7 (11.4)	4 (57.1)	3 (42.9)		12.6±4.9		71.3±3.6	
Moderate	20 (32.8)	11 (55.0)	9 (45.0)		12.2±4.5		72.8±13.3	
Severe	20 (32.8)	8 (40.0)	12 (60.0)		10.9±5.2		73.0±16.1	
Semitones	11.9±5.5	12.8±6.3	10.9±4.4	0.169	0.23±0.15*	0.121	−0.10±0.05*	0.063
SPL med (dB)	71.2±4.9	71.4±5.6	71.0±3.9	0.748	0.15±0.13*	0.243	0.04±0.05*	0.360
SPL max (dB)	80.2±7.3	80.0±7.7	80.4±7.0	0.842	0.30±0.19*	0.125	0.02±0.07*	0.798
Speech time (sec)	59.8±18.3	57.1±17.5	62.7±19.1	0.237	−0.60±0.50*	0.243	0.19±0.18*	0.292

Data are shown as mean±standard deviation or number (%).
AD: Alzheimer's disease, VD: vascular dementia, FTD: frontotemporal dementia, MCI: mild cognitive impairment, MMSE: Mini-Mental State Examination, SPL med: sound pressure level medium, SPL max: sound pressure level maximum.
*Oral reading was influenced by the presence of distractibility, hesitation, vocal fry, difficulty in word articulation, memory difficulty and altered prosody, which characterizes fronto-executive dysfunction; †Regression coefficient±standard error.

28.6% were subjects with FTD and 21.4% were diagnosed with VD. Furthermore, 35.7% of subjects diagnosed with impaired verbal reading skills had a "moderate" MMSE score and 64.3% a "severe" MMSE score.

All patients showed normal ENT status, even in the most serious cases of cognitive decline (moderate and severe) and difficulty in executing simple orders such as oral opening and tongue mobility.

Table 3 displays the relationship between MMSE score and the SRP parameters. As seen in **Table 2**, increased severity of the MMSE score led to a reduction in the average values of the semitones, average SPL and max SPL parameters and these differences are highly significant ($p<0.001$). Overall SPT, which is the time between the first and last syllable pronounced, was found to increase along with the increase in MMSE scores and this trend was statistically significant ($p<0.001$).

However, as shown inable produced. Overtones and **Table 4**, the association between the diagnoses of the subjects analyzed and the SRP parameters reveals that subjects with AD recorded the lowest average score in semitones, while those with MCI showed a lower average

Table 3. Comparison between MMSE scores and SRP parameters

SRP	MMSE				*p*-value
	Normal (n=14)	Mild (n=7)	Moderate (n=20)	Severe (n=20)	
Semitones	20.6±1.9	11.7±1.1*	10.6±2.8*	7.1±1.5*,†,‡	<0.001
SPL med (dB)	76.5±3.1	68.8±6.4*	67.3±4.4*	65.3±3.5*	<0.001
SPL max (dB)	85.9±6.9	79.9±8.2	76.1±6.9	72.5±4.2*	<0.001
Speech time (sec)	37.8±2.4	54.1±6.7	64.4±13.4	72.5±15.6*,†	<0.001

Data are shown as mean±standard deviation.
MMSE: Mini-Mental State Examination, SRP: speech range profile, SPL med: sound pressure level medium, SPL max: sound pressure level maximum.
*$p<0.05$ *post hoc* test vs. normal; †$p<0.05$ *post hoc* test vs. mild; ‡$p<0.05$ *post hoc* test vs. moderate.

Table 4. Comparison between the type of cognitive decline and SRP parameters

SRP	Diagnosis					*p*-value
	Healthy (n=14)	VD (n=11)	FTD (n=6)	MCI (n=12)	AD (n=18)	
Semitones	20.6±1.9	9.3±2.7*	9.0±0.9*	12.6±1.7*,‡,§	7.2±1.9*,†	<0.001
SPL med (dB)	76.5±3.1	69.0±5.6*	69.3±1.0*	68.8±4.7*	70.7±3.3*	<0.001
SPL max (dB)	85.9±6.9	77.8±7.7*	76.3±1.4*	78.7±6.3	79.4±7.3	0.014
Speech time (sec)	37.8±2.4	71.8±14.4*	70.0±8.9*	52.2±5.6*,‡,§	71.2±17.6*,†	<0.001

Data are shown as mean±standard deviation.
SRP: speech range profile, VD: vascular dementia, FTD: fronto-temporal dementia, MCI: mild cognitive impairment, AD: Alzheimer's disease, SPL med: sound pressure level medium, SPL max: sound pressure level maximum.
*p<0.05 *post hoc* test vs. healthy; †p<0.05 *post hoc* test vs. MCI; ‡p<0.05 *post hoc* test vs. FTD; §p<0.05 *post hoc* test vs. VD.

Table 5. Multiple linear regression analysis of the relationship between MMSE values and SRP parameters

SRP*	MMSE†	
	B-estimate (95% CI)	*p*-value
Semitones	0.851 (0.636, 0.907)	<0.001
SPL med (dB)	−0.148 (−0.320, 0.018)	0.079
SPL max (dB)	0.208 (0.036, 0.247)	0.010
Speech time (sec)	−0.092 (−0.063, 0.012)	0.187

MMSE: Mini-Mental State Examination, SRP: speech range profile, CI: confidence interval, SPL med: sound pressure level medium, SPL max: sound pressure level maximum.
*SRP: independent variables, †MMSE: dependent variable.

SPL value, and those with FTD recorded a lower average max SPL score. Subjects affected by VD and AD had the longest time between the first and last syllable pronounced. All the mean differences analyzed were statistically significant.

Multiple linear regression analysis revealed that 89.3% of the variance in MMSE was attributed to SRP parameters (R^2=0.893, p<0.001). The greatest predictivity of MMSE values emerged from the values of semitones (B=0.851; p<0.001) and the values of SPL max dB (B=0.208; p=0.010) (**Table 5**).

DISCUSSION

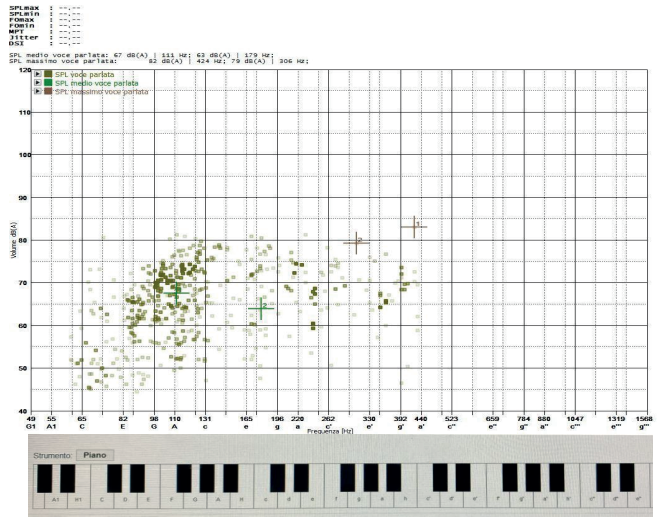
The increase in the elderly population worldwide has led to AD and other forms of cognitive decline.[21-26] The potentially modifiable risk factors for dementia include education, hypertension, diabetes, obesity, traumatic brain injury, smoking, alcohol abuse, air pollution, depression, physical inactivity[8] along with the three frequent otolaryngological conditions including oropharyngeal dysphagia,[2] unmanaged hearing loss[8,27] and vestibular dysfunction.[28,29]

Speech is the main channel of human communication and has great potential to monitor people with dementia. It is possible to identify behavioral markers of dementia variants based on the characteristics of speech and language.[30]

Accordingly, our study underscored several important features, including a significant reduction in the values of semitones directly proportional to the decrease in cognitive status (**Fig. 1A and B**) when compared with healthy subjects. A reduction in the prosody of speech was found in this class of subjects.

Prosody is a complex process that involves modulation of pitch, loudness, duration, and linearity in the acoustic stream to serve linguistic and affective communication goals.[31] Broadly speaking, prosodic goals include the transmission of linguistic and paralinguistic

A Healthy



B AD

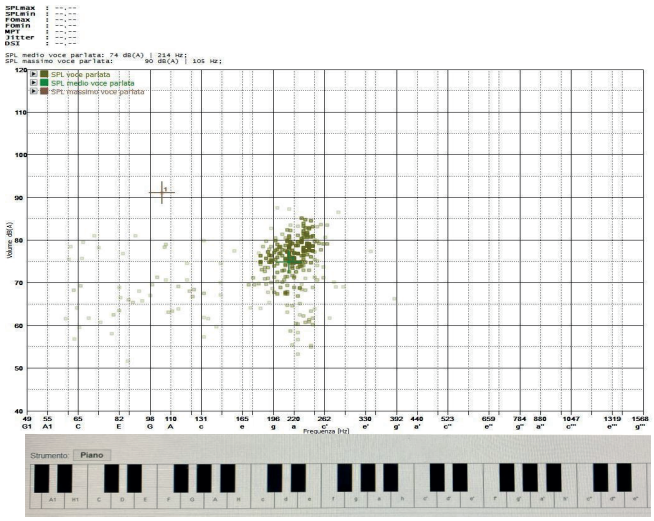


Fig. 1. (A) Healthy subjects showed an speech range profile of at least 20.8 semitones, (B) Subjects suffering from AD scored 7 semitones. As showed in Fig. 1A and 1B, the relationship between cognitive decline and the speech profile is represented by the reduction in the number of semitones.*
SPL max: sound pressure level maximum, SPL min: sound pressure level minimum, F0: fundamental frequency is the frequency at which vocal folds vibrate in voiced sounds, F0 max: maximum values of this frequency, F0 min: minimum values of this frequency, MPT: maximum phonation time, DSI: dysphonia severity index, AD: Alzheimer's disease.
*Semitone is the basic unit of measurement on a phonetogram. It is indicated by the half tone on the digital keyboard.

(emotional and attitudinal) information efficiently and pragmatically appropriate in a given language community.[31] For this reason, prosody is considered as a cognitive function. Therefore, we expected a decrease in prosody in patients suffering from dementia or MCI. We observed that healthy subjects showed an SRP of at least 20.8 semitones (**Fig 1A**), while in subjects affected by cognitive decline the values of semitones were reduced by at least 8 in cases of MCI and up to 13.4 less in patients suffering from AD (**Fig 1B**). As already mentioned earlier, the reduction in SRP semitone values was higher in subjects suffering from AD than in the other forms of dementia analyzed. Taler and Phillips[32] reported in a 2007 study that prosody was always impaired in elderly patients with AD, which was corroborated by other investigators.[33-35] Interestingly, a major decline in the productive and repetitive component of prosody occurs during the middle phase of AD despite a mild start.[36] This feature distinguishing AD from other forms of dementia may depend on the gradually variable, progressive involvement of the temporal, parietal and frontal regions.[36,37] However, many studies used different methods to analyze patients, such as simple psychological tests and audio recordings, some of which were subsequently analyzed with the free software PRAAT available for formatting and analyzing sound signals.[32-34]

In addiction, only one class of subjects suffering from one type of cognitive decline or MCI were reported.[38] For these reasons, the differences between our work and the other studies were important. We compared various types of cognitive decline based on SRP values determined using the latest software programs.

The analysis of the SPL parameters showed alterations in patients suffering from dementia compared with healthy subjects. The decrease in SPL max and SPL med parameters was similar for all forms of cognitive impairment, and was attributed to tremulous voice or slurred speech, with less intensity and less control of airflow, as reported widely in the literature[39,40] and confirmed by the computational values.

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The third parameter that was compromised in our study was the SPT measured in seconds. While the healthy subjects showed an SPT of 37.8 seconds, patients suffering from cognitive impairment showed an increase in SPT up to 70 seconds. This result was similar for all forms of dementia studied. Even though MCI patients showed an increase in SPT in comparison with the healthy subjects, it was less pronounced when compared with patients diagnosed with dementia.

We believe this feature is strictly linked to the impaired capacity for oral reading in our patients. Oral reading is influenced by distraction, hesitation, vocal fry, difficulty in word articulation, difficult in memory and altered prosody, which is associated with fronto-executive dysfunction.[41]

This retrospective observational study was limited by the the small number of participants in study and control groups, and thus associated with bias in the selection of patients from the same area and analysis at the same center.

However, SRP was easy to perform, rapid, non-invasive, and capable of highlighting the differences between the groups analyzed with cognitive decline. It was useful in elucidating the relationship between cognitive decline and speech profile to reveal useful diagnostic information of patients.

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