Journal of Kerman University of Medical Sciences

JKMU

Journal of Kerman University of Medical Sciences, 2018; 25 (2): 164-174

Oral and Laryngeal Diadochokinetic Rate in Multiple Sclerosis: Relationship to Disease Progression

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Received: 23 October, 2017 Accepted: 17 April, 2018

ARTICLE INFO

Article type:
Original article

Keywords:
Speech motor control
Multiple Sclerosis
Diadochokinesis

Abstract

Background: The first purpose of this study was to investigate the rate of oral and laryngeal Diadochokinesis (DDK) in Multiple Sclerosis (MS) patients in comparison with healthy people. The second goal was to determine if DDK rate has any relationship with the disease progression.

Methods: In this cross-sectional study, two groups were enrolled: MS patients (n=31) and healthy subjects (n=14). The samples of DDK tasks were collected. The scores of Expanded Disability Status Scale (EDSS) and duration of disease were considered as the indices of disease progression.

Results: There were significant differences between the two groups in the rates of all DDK tasks ($P \leq 0.001$). Significant correlations were found between laryngeal DDK tasks and disease progression ($r = -0.488$, $r = -0.396$, $r = -0.444$, $r = -0.667$, $P \leq 0.027$). Two oral DDK tasks were in correlation with EDSS and the disease duration ($r = -0.403$, $r = -0.446$, $r = -0.521$, $r = -0.465$, $p \leq 0.025$). There were high correlations between functional systems of EDSS (pyramidal, cerebellar and brainstem) and DDK tasks ($r = -0.448$, $r = -452$, $r = -0.458$, $r = -0.379$, $P \leq 0.036$).

Conclusions: In the present study, poor performance in DDK tasks provided evidence for insufficient motor control over related speech subsystems in MS. These findings suggest that DDK rate is a sensitive beneficial speech motor control assessment in MS. Moreover, DDK tasks might be introduced as additional prognostic parameters for detecting disease progression and evaluating treatment achievements.

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Citation: Ansari S, Soltani M, Moradi N, Rezai H, Latifi S.M, Majdinasab N. Oral and Laryngeal Diadochokinetic Rate in Multiple Sclerosis: Relationship to Disease Progression. Journal of Kerman University of Medical Sciences, 2018; 25 (2): 164-174.

Introduction

Speech is a unique motor achievement and the fastest discrete motor function of a human (1) which involves planning movements and preparing to execute them in order to achieve muscular contractions besides structural displacements (2). Speech motor control is a complex of systems and mechanisms that control speech production. It needs inputs and outputs for transferring the desired message. In this regard, phonological representations of language are the inputs and the outputs are articulatory movements. Indeed, speech motor control process has a mediating role between language formulation and acoustic signals (1). At the neuromotor level, speech subsystems (respiration, phonation, resonance, articulation) cooperate to produce harmonious kinematic patterns in a complex and dynamic biomechanical environment (3, 4).

Diadochokinesis (DDK) is a part of the standard neurological assessment of various body movements, including speech movements (5). It is the ability to perform the rapid repetition of relatively simple patterns of contrary muscular contractions (6).Traditionally, DDK is one of the most original tasks of speech motor assessment (5). In speech and language pathology, oral DDK involves the muscle contraction of jaw, lips, and tongue. There is another kind of DDK task, called laryngeal DDK that assesses the function at the level of vocal cords (7). Since syllable repetition in the verbal version of DDK reflects various places of articulation, rapid and accurate repetitions indicate a better control over the production of intended phonetic goals and a coordinated speech. DDK can evaluate the vital ability of the rapid and accurate programming of the sequences of basic speech movements (5, 6). It is a speech-like examination based on real syllables that detects respiratory-phonatory support (5, 7). Being nonsensitive to linguistic and cognitive deficits, it is a suitable index for investigating the underlying speech motor impairments in neurogenic diseases (5, 8). Currently, DDK is being used as a measure of speech function in neurological diseases such as Amyotrophic Lateral Sclerosis (ALS), Friedrich's disease, traumatic brain injury (TBI), and apraxia (8-12).

Speech production may be impaired following disturbances in the central motor system (13). Specific speech features of neurological diseases, such as DDK, can play a key role in the early diagnosis of them (14); for example, DDK in TBI has reflected the severity of brain damage and can be used as a prognostic parameter (9). Therefore, a valid clinical speech assessment plays an important role in evaluating and managing the progression of a neurological disease (6, 15). Multiple sclerosis (MS) patients are one of the clinical populations that can be considered by those interested in diagnosing the progression of neurological diseases through speech. MS is a common neuro-muscular progressive disease of unknown origin and usually begins in the third decade of life (3). There might be a relapse-remitting phase that consists of partial symptom remissions after periods of impairment. In some patients, it is represented as a chronic-progressive type which may start from the onset of disease or secondarily and is characterized by a continuous deterioration (16) affecting various functions such as ambulation, cognition and fine motor activities (3). Based on the literature, about 40-50% of individuals with MS show speech motor impairments characterized by respiratory support for speech production, deficits in pitch

variation, abnormally prolonged intervals, imprecise consonants, impaired loudness, dysphonia, prosody and stress as a result of various speech production components' that would be involved in the disease (17). Previous studies have provided evidence for the abnormal performance of oral DDK in MS patients and the low rate of oral DDK is known as a distinctive feature of speech motor function in MS (8, 18). But no study, to the authors' knowledge, has particularly reported the rate of laryngeal DDK tasks in this population. Also, a few studies so far have addressed the relationship between the results of speech assessments and the severity of neurological disability status in MS and contradictory results have been reported in this regard (19-22). EDSS is the most widely used diagnostic tool to assess the progression of MS. This scale is a non-linear ordinal combination of damage and disability and it includes the status of functional systems: pyramidal, cerebellar, sensory, visual, intestinal and bladder, and mental. With regard to the walking ability of patients, EDSS total score ranges from 0 to 10 (0 = without a disability, 10=death due to MS). Each functional system is graded from 0 to ۰ or 6, based on the severity (0 = normal, 5 or 6 = maximal impairment) (23). The aim of this study was primarily to investigate the performance of the MS patients in the rate of oral and laryngeal DDK comparing to the healthy control group, and secondly, to examine the relationship between DDK rate and the duration of the disease and EDSS score (23).

Methods

Participats

The present study was cross-sectional and non-experimental. Thirty one monolingual Persian-speaking MS patients (24 females, 7 males) and a matched control group of 14 normal subjects (8 females, 6 males) participated in this study. All MS patients in this study were in the relapse-remitting phase of MS.

Sampling was performed at Speech Therapy Clinic of Ahvaz Jundishapur University of Medical Sciences. The study protocol was approved by the Ethics Committee (IRAJUMS.REC.1395.615) and all participants signed the informed consent form. The patients' medical records were obtained from the Local Multiple Sclerosis Society. Patients with following criteria were enrolled in the study: received a diagnosis of MS disease approved by a neurologist, adults aged between 18 and 60 years (in order to avoid the effects of puberty and aging (24, 25)), no recent relapse, non-smoker, without a history of laryngeal or neurological surgery or intubation, having no voice problems unrelated to neurological diagnosis, having no history of receiving speech therapy interventions. The same criteria were adopted for the control group. The auditory system of all subjects was assessed during the perceptual conversation in an acoustic room.

Data collection

In this study, EDSS scoring was performed by a neurologist settled in the MS center. The number of years from onset of disease symptoms to evaluation day was considered as disease duration.

The assessment sessions were held in the early hours of the day, to prevent the effect of common fatigue on the performance of the patient group, by the same speech and

language pathologist. The experimenter explained the procedure for each participant at the beginning of each task and provided an example of the correct implementation. The participants were asked to repeat target syllables after a deep breath with their habitual pitch and loudness, as fast and steady as they could while maintaining the accuracy of the output until they were asked to stop. Each task continued for at least 3 to 5 seconds (7). The target syllables of laryngeal DDK, to evaluate the rate of vocal folds in repetitive laryngeal adduction and abduction movements in order to opening and closing vocal folds, were /ʔɑ/ and /hɑ/ (26). Syllables /pe/, /te/, /ke/, and /peteke/ were used for oral DDK. This order was the same for all the subjects (8, 27). Sound samples were recorded using a Shure microphone (BG 1.1 / C15AHZ / Pin2Hot), connected to a Dell 1545 laptop by using the Cubase5 software. The rate was defined as count by time (rate/2 sec) (28)and the number of the repeated syllables was counted in a two-second window in PRAAT software version 6/16 (29). The beginning of the time window was considered from the onset of the second repeated syllable. Partial syllables within the selected window were counted in the rate calculation (8).

Statistical Methods

SPSS 16 was used to perform statistical analyses. A non-parametric test of Kolmogorov-Smirnov was applied to analyze the distribution of data. The independent t-test was used to calculate the differences between the groups for variables with a normal distribution. Non-parametric statistical tests, Mann-Whitney and Spearman's rank correlation were used for non-normally distributed data in order to compare differences between the two groups and correlation analysis. In this study, p-values below 0.05 were considered significant.

Results

Descriptive data of participants

The descriptive data of EDSS score and disease duration have been presented in Table 1.

Table 1. characteristics of disease in the patient group

Group	Number	EDSS Score			Duration of disease (year)
		min	max	median	mean± SD
MS	31	0	5.5	1.5	5.3±4.2

Abbreviations: MS = Multiple Sclerosis; max = maximum; min = minimum; SD = standard deviation

Age group difference has been analyzed using independent t-test at the level of 0.05. There was no significant difference (p = 0.67, t = 0.42) between the MS group (mean = 37± 9.3(SD); range =18-55) and the control group (mean = 36± 1.1(SD); range = 21-57).

In this study, pyramidal, cerebellar, brainstem, and sensory functional systems had a median of 1(all ranged from 0 to 3). The median of optic and mental functional systems was 0 (range = 0 -۲ , range = 0 - 1, respectively).

Oral and laryngeal DDK in MS group compared to the control group

The average rates and standard deviations of oral and laryngeal DDK tasks for the MS patients and the control subjects have been displayed in Table 2. Moreover, results from comparing rate in the two groups were obtained using the Mann-Whitney test for abnormally distributed data (/pe/, /peteke/, /ʔɑ/ and /hɑ/) and independent t-test for those with a

normal distribution (/te/ and /ke/). As it is demonstrated, there were significant rate differences between the two groups for all DDK tasks (P ≤ 0.001), indicating the DDK rate in MS group was lower than the controls.

Table 2. Comparison between MS Patients and Control Group in the Rate of DDK Tasks

DDK task	MS Mean± SD	Control Mean±SD	P value
/ʔɑ/	3.38±1.03	4.92±0.93	<0.001*
/hɑ/	3.06±1.06	4.17±0.69	0.001*
/pe/	4.51±1.48	6.39±0.98	<0.001*
/te/	4.59±1.58	6.67±1.21	<0.001*
/ke/	4.19±1.47	6.14±0.79	<0.001*
/peteke/	2.12±0.51	2.75±0.50	0.001*

* Significant at 0.٠5 level
Abbreviations: MS = Multiple Sclerosis; DDK = Diadochokinetic; SD = standard deviation

The relationship of EDSS and disease duration with DDK rate

Results on the relationship between the rate of DDK and the features of MS disease have been presented in Table 3. The Spearman coefficient for the relationship between EDSS scores and repetition rate of syllables /ʔɑ/ and /hɑ/ showed significant correlations (P ≤ 0.027). These laryngeal DDK tasks were also in correlation with the disease duration (P ≤ 0.012). In addition, the rate of syllable /hɑ/ indicated significant correlations with pyramidal (P = 0.11), cerebellar (P = 0.01) and brainstem (P = 0.01) functions. The two oral DDK tasks, /ke/ and /peteke/, were highly correlated with MS disease duration (p ≤ 0.025) and EDSS scores (p ≤ 0.012). Also /peteke/ had significant correlation with pyramidal function of EDSS scale (p = 0.036). All the obtained correlations were negative (Table 4).

Table 3. Correlation of DDK Rate with Disease Duration and EDSS

DDK task	Disease Duration		EDSS	
	R	p value	r	p value
/ʔɑ/	-0.48	0.005*	-0.39	0.027*
/hɑ/	-0.44	0.012*	-0.66	<0.001*
/pe/	-0.31	0.084	-0.24	0.184
/te/	-0.33	0.066	-0.35	0.053
/ke/	-0.40	0.025*	-0.44	0.012*
/peteke/	-0.52	0.003*	-0.46	0.008*

* Correlation is significant at 0.05 (two tailed)
Abbreviations: DDK = Diadochokinesis; EDSS = Expanded Disability Status Scale; r = correlation coefficient

Table 4. Results of Correlation between DDK Rate and the Functional Systems of EDSS

Functional system	DDK task											
	/ʔɑ/		/hɑ/		/pe/		/te/		/ke/		/peteke/	
	r	p value	r	p value	r	p value	r	p value	R	p value	R	p value
Pyramidal	-0.28	0.127	-0.44	0.011*	-0.18	0.313	-0.18	0.331	-0.25	0.173	-0.37	0.036*
Cerebellar	-0.23	0.21	-0.45	0.011*	-0.04	0.81	-0.14	0.451	-0.14	0.442	-0.09	0.601
Brainstem	-0.14	0.449	-0.45	0.01*	-0.75	0.687	-0.07	0.671	-0.21	0.238	-0.34	0.056
Sensory	-0.02	0.886	-0.05	0.778	-0.13	0.455	-0.16	0.364	-0.20	0.264	-0.27	0.137
Blade& Bower	0.00	0.981	0.51	0.784	-0.16	0.374	0.01	0.939	0.06	0.717	-0.06	0.744
Optic	-0.12	0.51	-0.10	0.56	-0.18	0.309	-0.23	0.198	-0.19	0.3	0.05	0.756
Mental	-0.28	0.126	-0.27	0.128	-0.28	0.116	-0.28	0.117	-0.27	0.131	-0.30	0.096

* Correlation is significant at the 0.05 (two tailed).
DDK: Diadochokinesis, EDSS: Expanded Disability Status Scale; r = correlation coefficient

Discussion

The first goal of this study was to compare the function of the speech motor system of MS patients and normal subjects in relation to oral and laryngeal DDK. In agreement with previous studies, results indicated significantly lower repetition rate of all syllables of oral DDK in the MS group compared to the control group (8, 18). Neurologically, normal subjects can either reduce the displacement of the movements of the articulatory organs or increase their speed so that they can increase the rate of syllable production (9), an ability that seems to be impaired by MS. Konstantopoulos in a study of DDK among dysarthric MS patients considered a failure to accomplish antagonistic muscle contraction as the possible reason for the low DDK rate in MS patients (18). But, what could be the basis of this failure? Previously, Duffy referred to the cerebellum's role in feedforward cycle for explaining the DDK rate reduction. According to this explanation, following cerebellum impairment, cerebral cortex plays a more significant role in the control of movements, and because it is assumed that a cortical revision of motor program requires more time than what cerebellum does, the execution rate of DDK decreases. Similarly, this reduction could be because of the system's excessive reliance on sensory guidance or maybe due to employing feedback system (such as auditory feedback) instead of feedforward (7). This assumption has been supported by the results from fMRI studies in which researchers reported the cerebellum's association with the capability of rapid repetition of the syllables (13). On the other hand, evidence from Magnetic resonance imaging in aphasia revealed an association between the impairment of cortical areas (left lateral precentral gyrus), involved in storing or accessing the programs of motor-phoneme, and reduction in DDK rate. Researchers concluded the association was due to these functions' role in feedback control (30). In the case of MS disease, although it is classically known as a white matter disease, recent studies have reported the heavy involvement of grey matter (31), including the cortical areas (32) and mostly the grey matter of the cerebellum (33). In this regard, the impaired performance observed in the form of reduced rate of muscle contractions in our MS patients might be justifiable following the involvement of central regions related to feedback/feedforward system. Further research is needed to clarify the exact central neural mechanisms of controlling DDK tasks in MS patients by using neuroimaging technics.

The present study also compared the rate of laryngeal DDK in MS patients and the control group. Comparing to oral DDK, in the literature less attention has been paid to the study of laryngeal DDK in neurological diseases and in particular, no previous report of laryngeal DDK rate has been found in individuals with MS. The results of the present study showed that the rate of laryngeal DDK, similar to oral DDK, was significantly lower than the healthy subjects. Previously, Renout, in his study on amyotrophic lateral sclerosis (ALS), reported slowdowns in laryngeal DDK and explained them by the fact that patients consciously reduce the speed of the whole speech motor control system compensatorily, or as a strategy to preserve execution accuracy for having intelligible speech (11). This could be a possible explanation for the results found in the present study for MS group; since, participants were instructed to repeat syllables steadily with their habitual loudness and pitch and otherwise their performance was not accepted. This might have challenged them to reduce rate in order to keep accuracy. In addition to explanations that contributed slow oral DDK to central control systems of

speech apparatus, it is of note that the process of vocal folds' opening and closing highly depends on air pressure provided by expiratory muscles (34). It is known that MS causes weak inspiratory and expiratory musculature even in patients with mild disability severity (35). Putting these together, it can be concluded the laryngeal DDK, which requires high expiratory support, is sensitive to expiratory muscle insufficiencies in MS patients. The observed low laryngeal DDK rate revealed this variable could be considered as a source of useful information about the laryngeal function's efficiency in the phonation of individuals with MS.

Another goal of this study was to investigate the rate of the two types of DDK, oral and laryngeal, in relation to EDSS score and the duration of disease in MS. The results showed that both oral and laryngeal DDK tasks had significant negative correlations with EDSS and disease duration. The higher EDSS scores were correlated with slower DDK rates. In this regard, Darley previously linked dysarthria to the degree of neurological involvement of MS patients (36, 37). These results are in line with a cohort study by Hartelius et al on a large sample including 77 MS patients. In his study, the severity of the neurological disorder, measured by two EDSS and RFSS (Regional Functional System Score), had direct relationships with the severity of speech deficits identified in a clinical dysarthria assessment (using Queensland protocol) and perceptual speech analysis. The mentioned study had been conducted on a sample with the mean age of 66.6 (± 10) years (20). In the current study, in order to remove the effect of aging on the results of individuals' performance, a relatively younger population of MS patients (37.4 ± 9.3) was assessed and the previous results were confirmed. These results suggest that, generally, more severe neurological disability and longer duration of MS are associated with lower oral and laryngeal DDK rates, indicating more difficult motor control of speech organs including lips, tongue, palate, and larynx. On the other hand, in a study by Yamout et al, only the acoustic characteristics of voice symptoms (maximum phonation time, Shimmer, baseline frequencies, and habitual pitch) were investigated in relation to EDSS and the disease duration in MS. Among other voice-related variables, there was no correlation except for voice fatigue and EDSS. In Yamout's study, a "mild-moderate-severe" classification has been used instead of the exact EDSS scores in the correlation analysis. Also, for disease duration, instead of using the exact number of years, patients were categorized into two groups (more/less than ten years), which might reduce the accuracy of the final reports (21). Bauer et al, in an attempt to investigate the relationship of EDSS with subjective and perceptual speech changes, used two self-assessment voice questionnaires (VHI and VRQL) and GRBAS perceptual test data. Except for the asthenia item on the GRBAS scale, no other correlation with EDSS was found. The use of non-objective assessments in that study, which was referred to as a limitation of their work (19), may partly explain the contradiction of their results with the present study. Previous studies have shown that DDK pathomechanisms in neuromuscular disorders have an insignificant correlation with perceptual and acoustic measurements related to speech intelligibility (7, 20), and therefore the contradiction observed in the different studies may be a result of different intrinsic characteristics of the employed assessments. As reported in the results, the two oral syllables /ke/ and /peteke/ had correlations with EDSS. Comparing to other oral DDK tasks, these two are relatively more complex to articulate (/ke/ includes a back consonant /k/,

which provides less somatosensory feedback and /peteke/ is a challenging task because of its alternations in articulation placement during repetitions). This could make these two oral syllables more sensitive to disease effects and progression. Further, some recent studies suggest that in MS, weakness in respiratory muscles could be correlated with EDSS (35). Regarding the great reliance of DDK tasks on expiratory strength, the correlations between this measurement and EDSS could be explained.

In addition, the results of the present study showed correlations between the rate of some oral and laryngeal DDK tasks and the patient's scores in the pyramidal, cerebellar and brainstem functional systems of EDSS. Due to the limited correlations found here, a definitive interpretation cannot be made. However, as mentioned before, there is evidence that the related brain regions of these systems are somehow involved in the processes that control DDK tasks (13, 32, 38). These findings may support the assumption that although speech is a unique motor control function, its underlying motor control requirements involved in quasi-speech tasks such as DDK, are probably in some aspects commonly affected by the same factors as other functional systems.

This work had some limitations which could be addressed in future studies. The majority of MS patients were not available for another examination session thus no further speech or respiratory assessment were conducted here, however they could provide valuable information in the interpretation of the DDK results. The relatively small sample size and wide age range for both MS and control group were other limitations. Further future studies with larger samples and more diverse impaired functions are requiered to help to illustrate considered issues.

Conclusion

In summary, these findings show that some aspects of speech motor control are impaired in MS and confirm DDK as being a sensitive clinical diagnostic assessment of speech motor function. It seems that the rate of laryngeal DDK may, moreover, provide useful information about the impaired underlying mechanisms involved in speech motor control. Current results support the assumption that there might be a relationship between speech deterioration and the overall progression of MS disease. The rate of oral and laryngeal DDK probably can be used as a useful index in monitoring the progress of the disease, and determining the efficacy of treatment in MS and presumably other neurological diseases.

Source of funding

The source of data used in this paper was from M.Sc. thesis of Sepideh Ansari, Student of Ahvaz Jundishapur University of Medical Sciences; and financial support was provided by Ahvaz Jundishapur University of Medical Sciences. (Master Thesis grant no: pht-9518)

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