Speech symptoms associated with early signs of Shy Drager syndrome

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SUMMARY Speech disturbances reflecting impaired laryngeal control were found in ten patients whose autonomic dysfunction was associated with central neurological disease (Shy Drager Syndrome). In contrast, ten patients with progressive autonomic failure without evidence of CNS involvement had no difficulties on speech function tasks in comparison with normal controls. Presence of speech symptoms may aid in the clinical differentiation between patients with pure autonomic dysfunction and those with central neurological involvement.

Progressive autonomic failure may occur in isolation¹ or in association with central nervous system disorders such as Shy-Drager syndrome or Parkinson's disease.² Symptoms of autonomic failure include: orthostatic hypotension, constipation, incontinence, anhidrosis, impotence, xerostomia, and impaired vision. In some patients, the autonomic dysfunction may be accompanied by central neurological signs such as ataxia, incoordination, rigidity, bradykinesia, tremor, emotional lability, and regressive reflexes, and is referred to as Shy-Drager syndrome.³ These other neurological manifestations appear two to five years after the onset of the autonomic symptoms and gradually progress in severity.⁴ Patients with Shy-Drager syndrome may have olivo-ponto-cerebellar atrophy, striatal-nigral degeneration, or a combination of the two.⁵

Biochemical and pharmacological studies have distinguished between these separate clinical syndromes, idiopathic orthostatic hypotension and Shy Drager Syndrome.^{6,7} Since the prognosis and clinical course differs significantly it is important to differentiate between these two syndromes. Such differentiation is difficult in the early disease stages since similar autonomic symptoms are often present in both disorders prior to the appearance of other neurological abnormalities in the patients with Shy Drager syndrome.

Laryngeal stridor, phonatory disorders, and other

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motor speech disturbances are frequent in patients with Shy Drager syndrome.⁸ Respiratory failure requiring tracheostomy may result from bilateral paresis of vocal fold abductor muscles.⁹ Teravainen and Udd¹⁰ described one patient whose vocal cord paralysis occurred one year prior to the appearance of both autonomic and extrapyramidal symptoms. Electromyographic studies have indicated denervation of the posterior cricoarytenoid and interarytenoid laryngeal muscles; marked atrophy of the posterior cricoarytenoid muscle was found post-mortem in Shy Drager syndrome patients.^{11,12}

Clinical investigations of speech disturbances have not attempted to differentiate between patients with Shy Drager syndrome and with idiopathic orthostatic hypotension. Linebaugh¹³ found dysarthria in 35 of 80 patients with autonomic failure, while Thomas and Schirger¹⁴ reported speech disturbances in 11 of 30 such patients whom they studied. Unfortunately, the classification of patients in these studies is unclear. In the present study, experimental tasks assessing speech production were employed and objective measures made of six different speech functions in patients with idiopathic orthostatic hypotension and Shy Drager syndrome. We have distinguished between these patient groups on the basis of the objective speech and phonatory assessment.

Methods

Subjects

Ten consecutively admitted patients were included in each of two patient groups, idiopathic orthostatic hypotension and Shy Drager syndrome. All patients were admitted to

Table 1 Results of examination for signs of autonomic and central nervous system dysfunction in patients with idiopathic orthostatic hypotension and Shy Drager syndrome

	Idiopathic orthostatic hypertension										Shy drager syndrome									
Patient No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Sex	F	F	M	M	M	F	M	F	F	F	F	M	M	M	F	M	M	M	M	M
Age	48	54	72	66	59	69	70	40	32	64	45	63	56	54	51	52	55	56	68	38
Duration of Symptoms (yrs)	18	13	12	9	9	8	6	5	3	2	10	10	9	6	6	4	4	4	3-5	2
Constipation	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+
Neurogenic bladder	+	-	+	-	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+
Impotence or loss of libido	-	+	+	+	+	-	+	-	-	-	+	+	+	+	+	+	+	+	+	+
Decreased sweating	-	+	+	-	+	+	-	+	-	-	+	+	-	-	-	-	-	-	-	-
Blurred vision	+	-	-	-	+	-	-	+	+	-	-	+	+	+	+	-	-	-	+	+
Horner's syndrome	-	+	-	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
Rigidity	-	-	-	-	-	-	-	-	-	-	+	-	+	+	+	+	+	+	+	+
Bradykinesia	-	-	-	-	-	-	-	-	-	-	+	-	+	-	+	+	-	+	+	+
Tremor	-	-	-	-	-	-	-	-	-	-	+	-	+	+	+	+	+	+	+	+
Babinski	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	-	+	+	+
Emotional lability	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	-	-	-	+	+
Incoordination	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
Regressive reflexes	-	-	-	-	-	-	-	-	-	-	+	+	+	-	+	+	-	+	+	+

the National Institute of Health for investigation of orthostatic hypotension as previously described.⁷ Table 1 summarises the clinical characteristics of patients in both groups. The mean ages ($\pm$ SD) of the idiopathic orthostatic hypotension and Shy Drager syndrome patients were 57.5 ($\pm$ 13.9) and 53.8 ($\pm$ 8.4) years, respectively. Seven of the Shy Drager syndrome patients had clinical signs of striatal-nigral degeneration while three exhibited symptoms of olivo-ponto-cerebellar atrophy. Twenty normal controls without history of autonomic or central nervous system dysfunction or speech/language disorders were selected to match each of the patients for sex and within 3 years in age. Medication was discontinued for at least one week prior to testing. Complete medical and neurological examinations were performed independent of the speech recordings. The speech analyses were conducted independently and without knowledge of the results of the medical and neurological examinations.

Recording procedures

All subjects were able to tolerate sitting in a high backed chair for a 15 minute recording session. Speech was recorded on a Nagra IV-S tape recorder with a microphone 3 inches (7.5 cm) from the subject's mouth. The sound pressure level of a 1000 Hz tone recorded at the subject's microphone, was read with a sound level meter for calibration purposes. A thirteen minute instruction tape provided the speech items for imitation including: extended phonations of vowels, imitation of sentences at regular and fast speech rates, rapid repetition of vowels and syllables for 7 seconds, production of vowels and syllables as rapidly as possible after a click, imitation of pitch glide, imitation of intonation contours in a sentence, imitation of four loudness levels, and production of word boundary contrast, for example "blue bell" vs "bluebell." Further details of these tasks are provided in Ludlow and Bassich.^{15 16}

Speech analyses

All speech recordings were analysed acoustically without knowledge of subject identity or diagnosis. Sound spectrograms were measured for time and fundamental frequency with an x-y digitiser calibrated in hundredths of a second and Hertz. Graphic Level Recorder tracings were used to measure sound pressure level re: 20 micro Pascals.¹⁷ Research assistants performed these measures following extensive training to assure a minimum of 0.80 reliability.

Thirty acoustic measures previously found to be valid for assessing the speech of dysarthric patients,¹⁵ were made for each subject and are defined in the Appendix. These measures can be subgrouped into six categories:

Rate control Five measures assessed patients' abilities to change speaking rate and to rapidly initiate speech.

Speech articulation Six measures assessed patients' control of movements of oral structures for speech. Some variables assessed differences in speech rate in sounds requiring lip and tongue movement while others assessed the effects of different articulators on the latency of speech initiation.

Voicing control Six variables measured phonatory control and the coordination of laryngeal movements with those of other articulators.

Fundamental frequency control Five measures were made of the maximum range in fundamental frequency (Fo) in speech intonation.

Syllable timing control Three variables assessed patients' control of syllable lengths and pause durations to achieve stress contrasts in speech.

Intensity control Five variables measured the maximum range in intensity and intensity control during speech production.

Table 2 Mean Z-Scores, range and percent of impaired subjects and results of ANOVAs comparing 2 groups of patients with idiopathic orthostatic hypotension (IOH) and Shy Drager syndrome (SDS)

Acoustic measure	IOH group			SDS group			F	p of F
	Mean Z score	Range	Percent *impaired	Mean Z score	Range	Percent *impaired		
F ₀ variations in imitation of intonation contour	-0.27	-1.73 to +3.07	40%	-1.86	-2.34 to -0.37	90%	9.6	0.006
Soft to shout intensity range	-0.08	-1.24 to +1.08	0%	-3.36	-6.55 to -1.02	80%	30.0	0.001
Maximum intensity level	0.37	-0.75 to +1.39	0%	-1.61	-5.31 to +0.06	50%	12.9	0.002
Voicing changes during vowel repetitions	0.36	-2.26 to +3.62	20%	-1.77	-3.39 to -0.66	60%	10.6	0.004
Voicing changes during consonant repetitions	0.81	-0.60 to +2.50	0%	-0.58	-1.78 to +0.42	20%	12.7	0.002
Voicing errors for vowels	0.31	-0.03 to +0.58	0%	-3.29	-5.99 to -0.74	70%	28.3	0.001
Voicing errors for consonants	0.21	-0.36 to +0.36	0%	-0.30	-1.36 to +0.29	10%	6.4	0.02

*Percent of patients with Z of p < 0.10

Results

To determine whether patients with progressive autonomic failure without evidence of CNS involvement were impaired on measures of speech motor control, the idiopathic orthostatic hypotension patient group and the age and sex matched control group were compared on each of the speech function measures listed in the Appendix. There were a total of 30 measures grouped according to the six different speech functions of rate control, speech articulation, voicing control, fundamental frequency control, syllable timing control and intensity control. None of the one-way ANOVAs blocking on age with log data¹⁸ indicated statistically significant differences ($p < 0.02$) between the two groups on any of the 30 speech function measures. Therefore, the idiopathic orthostatic hypotension group had no difficulties on speech motor control tasks in comparison with normals.

Since the idiopathic orthostatic hypotension and Shy Drager syndrome patient groups differed in age, it was necessary to compute the degree of deviance of each subject relative to their age-matched control group to allow for comparisons between the two patient groups. Z scores were computed for each patient on each acoustic measure and indicated by what number of standard deviations a patient's score differed from normal and in which direction. Z scores of patients in the idiopathic orthostatic hypotension and Shy Drager syndrome groups were then compared by computing one-way ANOVAs¹⁸ for each speech function measure. Statistically significant differences ($p < 0.02$) were found on seven of the thirty measures. The ANOVA results are presented for these seven measures in table 2. The Shy Drager syndrome patients had more voicing errors and fewer voicing onsets and offsets during vowel and consonant repetitions. Although both groups had reduced Z scores indicating less change

in fundamental frequency than normal, the Shy Drager syndrome patients were significantly reduced in comparison with the idiopathic orthostatic hypotension group. The "soft" to "shout" intensity range was also significantly reduced in the Shy Drager syndrome group as was the maximum level of intensity on the loudness imitation task. Although significant differences were found between the idiopathic orthostatic hypotension and Shy Drager syndrome groups on seven of the speech function measures, the mean Z scores of subjects in the Shy Drager syndrome group were outside of the range of 90% of the normal controls on only five of these measures. The mean and range in Z scores and the percentage of patients with Z scores in the impaired direction for both patient groups on these seven measures are presented in table 2. Nine of the 10 Shy Drager syndrome patients had less fundamental frequency variation in sentence intonation than 90% of the normal controls. Similarly, eight of the Shy Drager syndrome patients were reduced in their maximum intensity range below the normal range, and five were reduced below the normal range in their maximum intensity level. Six of the Shy Drager syndrome patients had fewer voicing changes on vowel repetitions than normal; however, all but two of the Shy Drager syndrome patients had normal numbers of voicing changes on consonant syllable repetition. A similar pattern of impairment on vowels but not on consonants was also found for the two measures of voicing errors.

The Z scores of the idiopathic orthostatic hypotension patients fell outside of the 90% normal limit on only two of the acoustic measures. Four of the idiopathic orthostatic hypotension patients had reduced fundamental frequency variation in sentences below normals, although the magnitude of Z scores in the impaired direction was not as great as in the Shy Drager syndrome patients. Two idiopathic orthostatic hypotension patients had

Table 3 Results of discriminant function analysis with acoustic data between idiopathic orthostatic hypotension and Shy Drager syndrome patients

Eigenvalue	Canonical correlation	Wilks' Lambda	df	p of χ^2
3.285	0.88	0.23338	5	0.0004
Variables included in discriminant function				
Vowel voicing errors		-0.56662		
Number of on-off phonations for /a/		0.24377		
F ₀ variation for sentences		0.22274		
Intensity range from soft to shout		0.66575		
Maximum intensity level		-0.12596		

fewer voicing changes on vowel repetitions than 90% of normals. This reduction, however, was due to an overall reduction in syllable repetition rate in these two patients since neither had a greater number of voicing errors than normal.

Pearson product moment coefficients were computed between the number of years of symptom duration and Z scores on each of the speech measures to determine whether the degree of speech impairment in Shy Drager syndrome patients was related to symptom duration.

Statistically significant relationships ($p < 0.02$) were found on only two of the measures. The patients with longer symptom durations had slower rates of repetition of the syllable/pa/ ($r = -0.77$) and were more impaired on bisyllabic repetition/pa-ta/, than on monosyllabic repetition /pa/, ($r = -0.72$). None of the five measures significantly impaired in the Shy Drager syndrome group were related to symptom duration.

To determine whether acoustic measures of speech could correctly identify Shy Drager syndrome patients, Z scores for the five speech measures found impaired in Shy Drager syndrome patients were used to compute a discriminant function (Direct Method);¹⁹ F₀ variation in Imitation of Intonation Contour, Soft to Shout Intensity Range, Maximum Intensity Level, Vowel Voicing Errors, and Voicing Changes during Vowel Repetitions.

The resultant weighting coefficients are presented in table 3. The discriminant function yielded a Wilks' Lambda of 0.23338 equivalent to a Chi Square with a probability of less than 0.0004. The resultant discriminant function correctly classified all of the idiopathic orthostatic hypotension patients and nine of the 10 Shy Drager syndrome patients. The misclassified Shy Drager syndrome patient had the shortest symptom duration.

The speech performance of idiopathic orthostatic hypotension and Shy Drager syndrome patients with the shortest symptom duration in each group were compared to determine whether these five measures of speech function could accurately identify Shy Drager syndrome patients in the early stages. Five of the Shy Drager syndrome patients had symptom durations of less than five years while only two of the five idiopathic orthostatic hypotension patients with the shortest symptom durations had durations of less than five years. In table 4, an asterisk is placed opposite those speech measures where a patient's Z score fell outside the 90% region of the normal distribution. Three of the Shy Drager syndrome patients in the early stages of disease progression had Z scores which fell within the impaired region on three or more of the acoustic measures. Only one of the idiopathic orthostatic hypotension patients with a shorter symptom duration was impaired and on only one measure; F₀ variation on imitation of

Table 4 Acoustic measures on which Z scores are outside of 90% of normal distribution in five SDS and five IOH patients with shortest symptom durations

Acoustic Measure	SDS patients Patient No. No. Years Symptoms:	16	17	18	19	20	IOH patients				
		4	4	4	3.5	2	6	7	8	9	10
F ₀ Variation in imitation of contour		*	*		*	*			*		
Soft to shout intensity range		*	*	*	*						
Maximum intensity level		*	*								
Voicing errors for vowels		*	*								
Voicing changes during vowel repetitions		*			*						

*Patient's Z—score falls in impaired range: p of Z < 0.10.

sentence intonation contour. This variable was also impaired in three of the idiopathic orthostatic hypotension patients with longer symptom durations. The intensity range from soft to shout was impaired in four of the five Shy Drager syndrome patients in the early stages of disease progression, yet none of the ten idiopathic orthostatic hypotension patients had impaired Z scores on this measure. This variable also had the largest weighting coefficient value in the discriminant function.

Discussion

This study demonstrates that speech disturbances are found only in patients whose autonomic dysfunction is associated with central neurological disease. All of the impaired speech function measures assessed phonatory function. Phonatory disorders were evident early in Shy Drager syndrome. Only one Shy Drager syndrome patient was misclassified using a discriminant function analysis containing acoustic measures of phonatory function for speech. This patient had experienced symptoms of autonomic dysfunction for less than two years and was impaired on only one of the speech measures, but reported symptoms of vocal fold fatigue and hoarseness. None of the idiopathic orthostatic hypotension patients reported such speech problems.

The five measures which were impaired in the Shy Drager syndrome group were all measures of the maximum function of the larynx for phonation. For example, the ability to shout was reduced, although the Shy Drager syndrome patients demonstrated a normal intensity level during conversation. Likewise, the ability to achieve a wide variation in fundamental frequency while speaking was impaired. Increased vocal intensity requires the coordination of an increase in vocal fold tension to maintain closure with an increase in airflow. A wide variation in fundamental speech frequency also requires precise control of the laryngeal muscles which adjust vocal fold tension.¹⁹

Two other measures impaired in the Shy Drager syndrome patients also reflected impaired laryngeal control. The decrease in the rate of phonatory onsets and offsets during vowels and not consonants indicates impaired ability of the laryngeal musculature to interrupt the air flow at the level of the larynx. The intra-oral valving of the airstream during plosive consonants during syllable repetition, however, was unimpaired. The number of voicing errors during vowel repetition but not during consonant syllable repetition indicates that the difficulties in control are primarily in laryngeal function.

Our results suggest that acoustic measures of laryngeal control can be used as a noninvasive

adjunct in the clinical evaluation of patients with autonomic dysfunction. Presence of speech symptoms may aid in the differentiation between patients with pure autonomic dysfunction and those with central neurological involvement. Biochemical and/or pharmacological tests require invasive procedures and may not discriminate patients in the early stages of the disease. An increase in speech symptoms developed during the later stages of the disease only in the Shy Drager syndrome patients. Shy Drager syndrome patients with symptom durations greater than five years demonstrated a marked slowing of speech rate and a further deterioration on the measures of the laryngeal control. Involvement of tongue, lip, and palatal movements occurs in the later stages of Shy Drager syndrome. Shy Drager syndrome patients may be considered dysarthric only in the advanced stages of the disease, even though speech symptoms reflecting vocal fold incompetence appear early. Further longitudinal studies are needed to determine the precise pattern of breakdown in the motor speech system in this syndrome.

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Appendix

Definition of Acoustic Measures

Name of measure

Rate control

1. Time of Regular Rate Sentence Production
2. Time of Fast Rate Sentence Production
3. Difference in Time Between Regular and Fast Sentence Rates
4. Change in Rate for Repetition of syllable /pa/
5. Latency in Initiation of Vowel /a/

Speech articulation

6. Lip vs Tongue Phonations
7. Tongue Blade vs Back Phonations
8. Change in Number of Monosyllabic vs Bisyllabic Phoneme Repetitions
9. Change in Number of Vowel vs Consonant Phoneme Repetitions
10. Change in Initiation of Speech Between Vowel /a/ vs Bilabial Syllable /ba/
11. Difference in Initiation of Speech Between Vowel /a/ vs Velar CV Syllable /ga/

Voicing control:

12. Total Number of Voicing Errors for Vowel Repetitions
13. Total Number of Voicing Errors for Consonant Repetitions

Definition of measure

Total time (in seconds) for the regular rate productions of Sentences A and B.

Total time (in seconds) for the fast rate productions of Sentences A and B.

Time (in seconds) for sentence production at regular rate minus time at fast rate.

Number of syllables in last 1.5 s minus number of syllables in first 1.5 s during a 5.5 s period of repetition of the syllable /pa/. Negative values reflect a decreasing rate of repetition.

Number of milliseconds between click initiation and onset of phonation of the vowel /a/.

Average number of voicing offsets occurring within a 5 second period for /ta/ and /ka/ syllable repetitions minus the number of voicing offsets for /pa/ repetitions.

Average number of voicing offsets occurring within a 5 s period for /ta/ syllable repetitions minus number of voicing offsets for /ka/ repetitions.

Change in Rate during a 5.5 s repetition of the syllable /pa/ minus the change in rate during a 5.5 s repetition of the syllables /pa-ta/.

Change in rate during a 5.5 s repetition of the vowel /a/ minus the change in rate during a 5.5 s repetition of the syllable /pa/.

Number of milliseconds between click initiation and onset of phonation of the syllable /ba/ minus the number of milliseconds between click initiation and onset of phonation of the vowel /a/.

Number of milliseconds between click initiation and onset of the phonation of the syllable /ga/ minus the number of milliseconds between click initiation and onset of phonation of the vowel /a/.

The total number of vowel repetitions of /a/, /i/, /iu/ and /ua/ minus the total number of phonatory offsets occurring within these four repetitions; measured within a 5 s interval.

The total number of consonant repetitions for the syllables /pa/, /ta/, /ka/, /pa-ta/ and /pa-ka/ minus the total number of phonatory offsets occurring within these syllable repetitions, measured within a 5 s interval.

14. Voicing Differences for Repetition of Vowel Syllables /iu/ vs /ua/ Total number of phonatory offsets occurring within a 5 s repetition of the syllable /ua/ minus the number of phonatory offsets occurring during a 5 s repetition of the syllable /iu/.
 15. Voicing Differences Between Tense /i/ vs Lax /a/ Vowel Syllable Total number of phonatory offsets occurring within a 5 s repetition of the syllable /a/ minus the number of phonatory offsets occurring within a 5 s repetition of the syllable /i/.
 16. Number of Voicing Changes During Repetitions of Vowel /a/ Total number of phonatory offsets which occur during a 5 s repetition of the syllable /a/.
 17. Number of Voicing Changes During Repetitions of the Syllable /pa/ Total number of phonatory offsets which occur during a 5 s repetition of the syllable /pa/.
- Fundamental frequency control*
18. Average F_0 in sentences Average of peak F_0 (measured in hertz) on six nouns in three sentences (D_1 , E_1 , and F_1).
 19. F_0 range Difference in hertz between low and high points of an ascending vowel production divided by the average F_0 in sentences.
 20. F_0 Variation in Sentence (C) Average of high and low F_0 differences in intonation contour of Sentence C, divided by average F_0 in sentences (in hertz).
 21. F_0 Change for Stress Contrasts Sentence (D) Differences in peak F_0 (measured in hertz) between two words of equal stress minus the difference in peak F_0 between words of unequal stress, divided by the average F_0 in sentences.
(D) is the F_0 change for the words "bluebell" vs "bluebell", (F) is the F_0 change for the words "cross word" vs "crossword".
 22. F_0 for Stress Contrasts Difference between initiation of equally stressed nouns in sentences D_1 and E_1 , measured in seconds.
- Stress timing control*
23. Inter-word Interval Length Differences between initiation of syllables in compound nouns in sentences D_2 and E_2 , measured in seconds.
 24. Inter-syllable Interval Length Difference between interval for initiation of equally stressed nouns in sentence F_1 minus interval between initiation times of syllables in compound nouns in Sentence F_2 , measured in seconds.
 25. Change in Interval Length to Achieve Linguistic Contrast
- Intensity control*
26. Phonation Length Total length in seconds for extended vowel productions of /a/ and /i/ produced at comfortable intensity and F_0 .
 27. Average Intensity in Sentences Average of peak sound pressure level on final words in six sentences, measured in dB re: 20 μ Pa.
 28. Soft to Shout Intensity Range Difference between peak sound pressure level measured in dB re: 20 μ Pa on "shout" production minus that on "soft" production of the vowel /a/.
 29. Soft to Loud Intensity Range Difference between peak sound pressure level measured in dB re: 20 μ Pa on "loud" production minus that on "soft" production of the word "no".
 30. Maximum Intensity Level Peak sound pressure level in dB re: 20 μ Pa on "shout" production of the vowel /a/.