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Dysarthria in Friedreich's Ataxia: A Perceptual Analysis

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Key Words
Friedreich's ataxia · Dysarthria · Perceptual analysis

Abstract
The aims of this study were to: (1) evaluate the perceptual speech dimensions, speech intelligibility and dysarthria severity of a group of individuals diagnosed with Friedreich's ataxia (FRDA); (2) determine the presence of subgroups within FRDA dysarthria; (3) investigate the relationship between the speech outcome and the clinical factors of disease progression. The study included 38 individuals (21 female, 17 male) with a confirmed diagnosis of FRDA. A group of 20 non-neurologically impaired individuals served as controls. Perceptual analysis, investigating 30 different dimensions of speech, was conducted on a speech sample obtained from each participant. In addition, the Assessment of Intelligibility of Dysarthria Speech was administered. All FRDA participants presented with dysarthria with severities ranging from mild to moderate. Cluster analysis revealed 3 subgroups, the first presenting with mild dysarthric symptoms, the second with increased velopharyngeal involvement and the third characterized by increased laryngeal dysfunction. Dysarthria severity showed a significant correlation to disease duration but to no other clinical measure. The findings support the notion of subgroups in FRDA dysarthria, representing distinct impairments of the speech mechanism and perhaps reflective of differing evolutions beyond the cerebellum.

Introduction

Dysarthria is a cardinal feature of Friedreich's ataxia (FRDA), a spinocerebellar neurodegenerative disorder and the most common of the hereditary ataxias. While the dysarthria in FRDA has been classically described in the literature as ataxic (associated with impairment of the cerebellum and its connections), the site of neurological impairment in FRDA has been reported to extended beyond the cerebellum, involving lesions in the posterior columns of the spinal cord, spinocerebellar tracts, dorsal columns, nuclei of the brainstem, pyramidal tracts, corticospinal motor tracts, and cranial and peripheral nerves [1, 2]. Therefore, it can be expected that the dysarthria associated with FRDA is not always purely ataxic in nature, but rather involves a mix of ataxic/spastic/flaccid components perhaps particularly as the disease progresses.

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Joanette and Dudley [3] suggested that the speech disorder in FRDA was reflective of a heterogenous set of speech dysfunctions rather than a single neurological entity. They presented 2 distinct groups of speech patterns – a 'general dysarthria factor' relating to articulation and a 'phonatory stenosis factor' relating to laryngeal function. They proposed that their findings of the dichotomous grouping of their FRDA participants represent 2 distinct evolutions of the same underlying pathology. Although not well defined, is it expected that the variations in the dysarthria in FRDA can be in part attributed to the stage of disease progression [3–5] and perhaps the result of both individual variability and variability over the course of the disease [5]. Further investigation into the dysarthria associated with FRDA in relation to disease progression may provide important insights into the nature of the evolution of FRDA.

The aims of this study, therefore, were to: (1) evaluate the speech function in a group of 38 individuals with FRDA by perceptual analysis, using well-defined and replicable scales; (2) determine the existence of subgroups within FRDA dysarthria; (3) investigate the relationship between the speech outcome and clinical factors of disease progression.

Methods

Participants

The study included 38 individuals (21 female, 17 male) diagnosed with FRDA with a mean age of 37.34 years (SD = 9.28, range = 23–58 years). Five participants were considered late-onset FRDA (i.e. after 21 years [6]). All participants, except 1, had molecular testing of the GAA repeat length and all were homozygous for a GAA repeat expansion. The subject who did not have genetic testing has a sibling with FRDA shown to be due to homozygosity for FXN GAA expansions. The Friedreich's Ataxia Rating Scale (FARS) [7], a measure of overall disease severity was administered to 26 participants by a neurologist and a clinical geneticist from the Monash Medical Centre, Vic., Australia. Biographical details for the FRDA subject group are listed in table 1. Individuals were excluded from the study if they had history of a speech disorder prior to the onset of FRDA or a prior/co-existing neurological disorder. A group of 20 non-neurologically impaired individuals (8 male and 12 female) served as controls. The mean age of the control group was 35.7 years (SD = 11.16, range = 22–58 years). All controls had perceptually normal speech, as judged by an experienced speech-language pathologist. All participants were native speakers of English.

Procedure

A recorded speech sample consisting of a reading of 'the grandfather passage' [8] was obtained from each subject for the purpose of perceptual analysis. In addition, the Assessment of Intelligibility of Dysarthria Speech (ASSIDS) [9] was administered to each participant according to the procedure specified in the manual, and recorded for later analysis. The recordings were collected using the digital Alexis Masterlink (ML-9600) with a head-set microphone (AKGModel C420) positioned 10 cm to the side of the mouth.

Table 1. Biographical and clinical details of the FRDA group

Subject No.	Age years	Gender	Age of onset years	Duration years	GAA1	GAA2	FARS score[1]
1	53	F	26	27	332	941	93.00
2	35	F	14	21	n.a.	n.a.	n.a.
3	41	M	14	27	800	1,100	n.a.
4	44	F	20	24	751	1,027	85.83
5	47	F	20	27	1,077	1,077	103.30
6	36	F	27	9	590	956	73.50
7	56	F	10	46	489	1,207	123.50
8	49	M	13	36	676	873	128.50
9	34	M	7	27	750	1,220	n.a.
10	29	F	10	25	938	938	117.50
11	38	M	13	25	480	870	n.a.
12	29	M	13	16	326	730	59.00
13	34	M	23	11	554	992	78.50
14	25	F	8	17	634	1,032	120.00
15	26	F	20	6	700	1,010	72.00
16	44	F	11	33	763	763	127.00
17	45	M	28	17	606	986	85.80
18	37	M	14	23	650	900	126.50
19	38	M	13	25	674	903	101.00
20	23	F	18	5	447	967	77.00
21	41	M	26	15	560	989	94.83
22	43	M	7	36	780	980	n.a.
23	31	F	8	23	642	1,132	127.00
24	39	F	10	29	706	706	n.a.
25	58	M	16	42	318	1,015	117.00
26	49	F	16	33	630	850	114.00
27	43	F	17	26	589	589	n.a.
28	33	F	14	19	853	853	n.a.
29	41	M	32	9	323	1,046	n.a.
30	36	F	13	23	706	811	108.00
31	42	F	20	22	646	1,293	108.00
32	23	F	7	16	508	711	n.a.
33	28	F	14	14	780	1,015	95.50
34	23	M	15	8	720	720	54.50
35	23	M	14	9	720	720	47.50
36	42	F	14	28	767	917	n.a.
37	30	M	9	21	253	1,088	n.a.
38	30	M	21	9	527	1,058	62.50

GAA1 = GAA expansion size on smaller allele of the *FXN* gene; GAA2 = GAA expansion size on larger allele of the *FXN* gene.

[1] Total score = 0–159 (higher score indicates greater disability).

Table 2. Perceptual speech assessments (significant results)

	FRDA (n = 38)	Control (n = 20)	Difference between means	U	p
Speech dimension					
Prosodic features					
Variation of pitch	1.95 ± 0.84	1.05 ± 0.22	0.90	135.0	<0.001
Variation of loudness	1.58 ± 0.72	1.00 ± 0.00	0.58	200.0	<0.001
Maintenance of loudness	1.79 ± 0.81	1.00 ± 0.00	0.79	160.0	<0.001
Phrase length	1.82 ± 0.80	1.00 ± 0.00	0.82	150.0	<0.001
General rate[1]	3.45 ± 0.80	4.20 ± 0.41	0.75	178.0	<0.001
Stress	1.87 ± 0.81	1.00 ± 0.00	0.87	130.0	<0.001
Respiratory features					
Breath support for speech	1.74 ± 0.79	1.00 ± 0.00	0.74	170.0	<0.001
Phonatory features					
Strain-strangled	1.58 ± 0.68	1.05 ± 0.22	0.53	217.0	0.001
Resonance					
Hypernasality	1.74 ± 0.86	1.05 ± 0.22	0.69	196.0	<0.001
Articulatory features					
Consonant precision	2.18 ± 0.46	1.00 ± 0.00	1.18	10.0	<0.001
Intelligibility					
Overall intelligibility	2.29 ± 0.46	1.00 ± 0.00	1.29	0.0	<0.001
ASSIDS					
Sentence intelligibility, %	96.37 ± 4.14	99.60 ± 0.38	3.23	63.50	<0.001
Total words per min	123.16 ± 29.95	194.71 ± 21.02	71.55	9.00	<0.001
Intelligible words per min	119.36 ± 30.90	193.90 ± 20.57	74.54	12.00	<0.001
CER	0.63 ± 0.16	1.02 ± 0.11	0.39	8.50	<0.001

Data presented as means ± SD. Significance set at $p < 0.002$ according to modified Bonferroni procedure. Speech dimensions rated on a 5-point interval scale (1 = no impairment). CER = Communicative efficiency ratio.
[1] Using a balanced 7-point scale (4 = normal).

The recorded samples were de-identified and randomized before being rated independently by 2 speech-language pathologists on a series of 30 speech dimensions encompassing prosody, respiration, phonation, resonance and articulation, based on those used by Darley et al. [10]. The judges conferred to produce a single consensus rating for each of the speech dimensions and for overall dysarthria severity, which were used in subsequent analysis. Inter-judge reliability was calculated using Spearman's ρ rank correlations ($\rho = 0.910$) and intra-judge reliability was determined by having each judge independently re-rate the speech samples of 8 (20%) randomly selected and de-identified participants (percentage of agreement = 88.71% for judge 1 and judge 2). The recordings of the ASSIDS were transcribed and scored by 2 independent judges who were unfamiliar with the participants, and separate to the judges who performed the perceptual ratings of the speech sample. The scores for the 2 judges were combined and averaged to obtain a mean which was used for further analysis. Inter-judge reliability using Pearson's r correlation coefficient revealed a high degree of intra-rater reliability for judge 1 ($r = 0.941$, $p < 0.01$) and judge 2 ($r = 0.920$, $p < 0.01$).

Results

The consensus perceptual ratings and the ASSIDS scores for the FRDA and control participants were compared using a Mann-Whitney U test for independent measures employing a modified Bonferroni procedure [11] to control for type 1 error. The significant results from this comparison are presented in table 2. All FRDA participants were classified as presenting with dysarthria, with overall dysarthria severity scores ranging from 2 (minimal dysarthria) to 5 (moderate dysarthria), with a group mean score of 3.03 (SD = 0.75).

In accordance with the suggestion that subgroups may exist in the dysarthria associated with FRDA [3, 5], the data from the FRDA group was subjected to an agglomerative hierarchical cluster analysis using complete linkage to define and compare the speech profile of each subgroup and compare the clinical features between subgroups. The 10 speech dimensions from the speech

Table 3. Speech profiles for control subjects, the 3 FRDA subgroups and the 3 individual FRDA subjects

	Control (n = 20)	Subgroup 1 (n = 26)	Subgroup 2 (n = 4)	Subgroup 3 (n = 5)	Subject 9 (n = 1)	Subject 16 (n = 1)	Subject 37 (n = 1)
Speech dimensions							
Variation of pitch	1.05 ± 0.22	1.62 ± 0.50	3.00 ± 0.00	2.20 ± 0.84	4.00	1.00	4.00
Variation of loudness	1.00 ± 0.00	1.31 ± 0.47	2.25 ± 0.50	1.80 ± 0.45	3.00	1.00	4.00
Maintenance of loudness	1.00 ± 0.00	1.50 ± 0.58	2.50 ± 0.58	2.20 ± 0.84	3.00	4.00	1.00
Phrase length	1.00 ± 0.00	1.42 ± 0.50	2.75 ± 0.50	2.40 ± 0.55	4.00	2.00	3.00
General rate[1]	4.20 ± 0.41	3.85 ± 0.46	2.50 ± 0.58	3.00 ± 0.00	2.00	3.00	1.00
Stress	1.00 ± 0.00	1.62 ± 0.57	2.25 ± 0.50	2.20 ± 0.74	4.00	1.00	4.00
Breath support for speech	1.00 ± 0.00	1.38 ± 0.50	2.75 ± 0.50	2.40 ± 0.55	4.00	2.00	1.00
Strain-strangled	1.05 ± 0.22	1.38 ± 0.57	2.00 ± 0.00	2.60 ± 0.55	1.00	1.00	1.00
Hypernasality	1.05 ± 0.22	1.58 ± 0.64	3.50 ± 0.58	1.20 ± 0.45	2.00	2.00	1.00
Consonant precision	1.00 ± 0.00	2.12 ± 0.33	2.75 ± 0.50	2.20 ± 0.45	3.00	1.00	2.00
Overall dysarthria severity[2]	1.00 ± 0.00	2.65 ± 0.49	4.25 ± 0.50	3.60 ± 0.55	4.00	3.00	4.00
ASSIDS							
Sentence intelligibility, %	99.60 ± 0.38	97.74 ± 1.86	95.63 ± 2.86	93.59 ± 6.91	82.73	98.86	90.23
CER	1.02 ± 0.11	0.71 ± 0.10	0.48 ± 0.02	0.52 ± 0.11	0.20	0.53	0.25

Data presented as means ± SD. Speech dimensions rated on a 5-point interval scale (1 = no impairment). CER = Communicative efficiency ratio.

[1] Using a balanced 7-point scale (4 = normal). [2] Using a 7-point scale (1 = no dysarthria).

sample analysis that were found to be significantly different compared to the control group were used to define the clusters. The cluster analysis identified the presence of 6 subgroups of FRDA participants. The clusters included 1 main subgroup (n = 26) with 2 smaller subgroups (n = 5, n = 4), and 3 outlying individuals (subjects 9, 16 and 37) remaining isolated from all other FRDA subjects and thus each forming a subgroup of their own. The speech profiles – as described by the means and SD of the 10 speech dimensions, the overall severity rating, and the measure of sentence intelligibility and communicative efficiency (as acquired from the ASSIDS for the control group, the 3 FRDA subgroups and the 3 outlying FRDA participants) – are presented in table 3. To further define the difference between subgroups within the FRDA group, the 3 outlying participants were removed and the 3 subgroups were compared using Mann-Whitney U tests. The results of these comparisons are presented in table 4.

To investigate the relationship of FRDA and its progression on speech outcome, a Spearman's ρ rank correlation was calculated to define the relationship between the clinical details of age of onset, disease duration, FARS score and genetic mutation (GAA1 and GAA2 values) with the perceptual measure of dysarthria severity. The results identified a significant correlation between dysarthria severity and disease duration ($\rho = 0.515$; $p = 0.001$), GAA2 ($\rho = 0.360$; $p = 0.028$) and FARS score ($\rho = 0.0.517$; $p = 0.007$). To compare the clinical factors across the 3 FRDA subgroups, a series of one-way ANOVAs were used. The analyses revealed only the measure of disease duration to be significant across the 3 subgroups ($F_{2, 34} = 5.013$; $p = 0.013$). Post hoc analysis showed a significant ($p = 0.019$) difference between subgroups 1 and 2 for disease duration, with subgroup 2 having a longer disease duration compared to subgroup 1.

Discussion

The cluster analysis identified the existence of 3 subgroups of FRDA participants differentiated according to their speech profiles. Additional to the 3 subgroups, 3 outlying participants emerged, reflecting the variability that exists in the dysarthria of FRDA. Subgroup 1 was the primary group, consisting of the majority (68%) of FRDA participants. This subgroup was characterized by mild impairments on 6 of the 10 dimensions, including consonant imprecision, reduced pitch variation, loudness maintenance, reduced phrase length, reduced breath support for speech and hypernasality, with a mild reduction in sentence intelligibility and communicative efficiency.

Table 4. Comparison between subgroups 1, 2 and 3

	Subgroup 1 vs. subgroup 2		Subgroup 1 vs. subgroup 3		Subgroup 2 vs. subgroup 3	
	U	p	U	p	U	p
Speech dimensions						
Variation of pitch	0.00	<0.001	37.00	0.144	4.00	0.190
Variation of loudness	12.00	0.011	33.00	0.091	6.00	0.413
Maintenance of loudness	14.00	0.180	33.00	0.091	8.00	0.730
Phrase length	5.50	0.001	16.50	0.006	6.50	0.413
General rate[1]	5.00	0.001	12.50	0.002[1]	5.00	0.286
Stress	5.00	0.094	37.50	0.144	10.00	1.000
Breath support for speech	5.00	0.001	15.55	0.005	6.50	0.413
Strain-strangled	20.00	0.052	11.50	0.002[1]	4.00	0.190
Hypernasality	2.00	<0.001	44.50	0.280	0.00	0.016
Consonant precision	19.00	0.044	59.50	0.775	4.50	0.190
Overall dysarthria severity[2]	0.00	<0.001	17.00	0.007	4.50	0.190
ASSIDS						
Sentence intelligibility, %	23.00	0.095	30.00	0.074	10.00	1.000
CER	4.00	0.001	13.00	0.004[1]	8.00	0.730

Significance st at $p < 0.004$ according to modified Bonferroni procedure. Speech dimensions rated on a 5-point interval scale (1 = no impairment). CER = Communicative efficiency ratio.

[1] Using a balanced 7-point scale (4 = normal). [2] Using a 7-point scale (1 = no dysarthria).

The articulatory dimension of consonant imprecision was the most affected speech feature in this subgroup, consistent with the 'general dysarthria factor' described by Joanette and Dudley [3].

The remaining 2 subgroups reflected more severe dysarthric impairments, with each group significantly differing from the primary subgroup with regards to overall dysarthria severity, general rate of speech and the functional measure of communicative efficiency. Subgroup 2 was further characterized by significantly reduced pitch variation, reduced phrase length, reduced breath support for speech and increased hypernasality, features reflective of velopharyngeal incompetence. In contrast, subgroup 3 featured increased strain strangled vocal quality with a low rating for hypernasality. This subgroup represented a phonatory disturbance of effortful voice production, reflecting a disturbance to the laryngeal mechanism. The clustering of these 2 subgroups was suggestive of the existence of 2 separate speech subgroups relating to distinct impairments in the speech mechanisms.

While the existence of subgroups relating to distinct speech mechanisms is consistent with the findings of Joanette and Dudley [3], the nature of the groupings varied. These authors indentified 2 factors within their group of 22 participants, a 'general dysarthria factor' reflecting prominently articulatory dysfunction and a 'phonatory stenosis factor' relating to laryngeal dysfunction. In the present study, articulatory function did not differentiate between the subgroups. A subgroup did exist that was defined by a phonatory impairment similar to the 'phonatory stenosis' of Joanette and Dudley [3]. Additionally, a subgroup was formed which was characterized by hypernasality and poor breath support for speech reflecting a velopharyngeal incompetence. Furthermore, the studies differed in relation to the reported dysarthria severities. The largest group in the study by Joanette and Dudley [3] presented with low intelligibility and severe dysarthric symptoms, in contrast to the present study where 68% of participants presented with very mild dysarthric symptoms. With severity classifications that are not well defined, it is difficult to compare to the present study. In regards to the clinical factors of the participants in each of the studies, the ages of participants were comparable; however, disease duration was defined differently between the 2 studies. Joanette and Dudley [3] calculated disease duration from time of initial diagnosis, compared to the present study that reports disease duration from first symptoms. For this reason, the reported severity of the dysarthria and the relationship to disease progression is unable to be compared between the 2 studies. The discrepancies in reported dysarthria severity and perceptual speech profiles could be related to the use of different

tasks and rating scales. Joanette and Dudley [3] conducted perceptual analysis on a sample of conversational speech, while a reading passage was used in the present study. Differences in the nature of the task and the demands involved may emphasize different speech features and result in discrepancies in the perceived dysarthria severities [12].

Joanette and Dudley [3] suggested that their finding of 2 distinct subgroups within FRDA dysarthria is indicative of distinct evolutions of the same underlying pathology. They further defined this as the presence of 'general involvement of the cerebellar systems and, in addition, a component which selectively affects one or more cranial nerve nuclei or their afferences' (p. 49). This notion could be applied to the groupings identified in the current study. The primary group presented with only mild dysarthric symptoms that are consistent with ataxic dysarthria and cerebellar lesions, with the remaining 2 subgroups perhaps reflecting 2 differing evolutions beyond the cerebellum, e.g. involving the corticobulbar tracts [13] or cranial nerve nuclei [14, 15].

Dysarthria severity correlated to disease duration and overall disease severity (FARS score), suggesting that the severity of dysarthria increased with increased disease duration. A number of studies have suggested a clear relationship between GAA expansion size and phenotype variability with the size of the smaller GAA expansion (GAA1 allele) being the major determining factor for the variability in age of onset and rate of disease progression [16–18]. Dürr et al. [16] reported an inverse relationship between the size of the smaller GAA 1 repeat and the age of onset in a study of 187 FRDA participants. In the present study, the size of the GAA1 expansion did not significantly correlate to dysarthria severity. The GAA2 (the larger allele), however, showed a positive but weak relationship with dysarthria severity, indicating that a greater number of expansions of GAA2 correlated with a severer dysarthria rating.

In conclusion, the results of this perceptual investigation support the notion that subgroups exist in the dysarthria in FRDA, varying in regards to the overall severity of the speech disorder and in terms of increased impairment of velopharyngeal or laryngeal function. The majority of FRDA participants in the current study presented with a mild dysarthria. Correlation analysis indicated a relationship between dysarthria severity and disease duration. The 2 subgroups presenting with a more severe speech disorder were distinguished by the presence of increased velopharyngeal versus laryngeal involvement perhaps reflective of differing underlying neuropathologies.

An investigation of the change in speech production over time in individuals with FRDA may provide a clearer picture of the evolution of the speech disorder in this population, and may assist in the prediction of disease progression. Furthermore, there is a need for widely accepted measures for longitudinal clinical outcomes in FRDA [19]. As the underlying pathogenesis of FRDA is understood and possible therapeutic agents are tested, the development of clinical outcome measures enabling accurate measurement of the benefits of therapeutic intervention is crucial. The present study has provided a comprehensive perceptual analysis of the speech function in FRDA on which a longitudinal study can be developed.

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