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Clinical and imaging characterization of progressive spastic dysarthria

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Abstract

Objective—To describe speech, neurological and imaging characteristics of a series of patients presenting with progressive spastic dysarthria (PSD) as the first and predominant sign of a presumed neurodegenerative disease.

Methods—Participants were 25 patients with spastic dysarthria as the only or predominant speech disorder. Clinical features, pattern of MRI volume loss on voxel-based morphometry, and pattern of hypometabolism with F18-Fluorodeoxyglucose (FDG-PET) scan are described.

Results—All patients demonstrated speech characteristics consistent with spastic dysarthria, including strained voice quality, slow speaking rate, monopitch and monoloudness, and slow and regular speech alternating motion rates. Eight patients did not have additional neurological findings on examination. Pseudobulbar affect, upper motor neuron pattern limb weakness, spasticity, Hoffman sign and positive Babinski reflexes were noted in some of the remaining patients. Twenty-three patients had electromyographic assessment and none had diffuse motor neuron disease or met El Escorial criteria for ALS. Voxel-based morphometry revealed striking bilateral white matter volume loss, affecting the motor cortex (BA 4), including the frontoparietal operculum (BA 43) with extension into the middle cerebral peduncle. FDG-PET showed subtle hypometabolism affecting the premotor and motor cortices in some patients, particularly in those who had a disease duration longer than two years.

Conclusions—We have characterized a neurodegenerative disorder that begins focally with spastic dysarthria due to involvement of the motor and premotor cortex and descending corticospinal and corticobulbar pathways. We propose the descriptive label “progressive spastic dysarthria” to best capture the dominant presenting feature of the syndrome.

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Keywords

dysarthria; neuromuscular disease; MRI; PET

Introduction

Progressive speech impairment (dysarthria, apraxia of speech) is not uncommon as a presenting complaint heralding neurodegenerative disease(1). Unique patterns of speech impairment are associated with specific sites of lesion and may inform the neurologic differential diagnosis(1, 2). For example, ataxic dysarthria is typically associated with lesions in the cerebellum(3) or its efferent or afferent pathways hypokinetic dysarthria with basal ganglia control circuit dysfunction, and spastic dysarthria with bilateral upper motor neuron lesions (see Kent(4) for review).

Some patterns of progressive dysarthria strongly suggest particular underlying pathology. A prime example is mixed spastic-flaccid dysarthria commonly associated with amyotrophic lateral sclerosis (ALS)(2, 5); about 20% of ALS cases present with bulbar signs, among which dysarthria is usually the most prominent(6, 7). In some patients, speech symptoms at initial evaluation reflect an isolated spastic or flaccid dysarthria that typically evolves to include both upper and lower motor neuron (LMN) features(8) (i.e., mixed spastic-flaccid dysarthria). Other patients eventually exhibit speech and/or nonspeech signs that establish a diagnosis other than ALS (e.g., corticobasal syndrome, progressive supranuclear palsy syndrome). However, an apparently small number of patients presenting with isolated progressive spastic dysarthria (PSD) do not develop additional symptoms to warrant these diagnoses. In such cases, the spastic dysarthria may represent primary lateral sclerosis (PLS) or a neurodegenerative variant of a rare motor syndrome such as anterior opercular syndrome, also known as Foix-Chavany-Marie syndrome(9–11). One barrier to a fuller understanding of PSD and its possible explanation is the sparse description of the specific speech attributes that characterize it, its other clinical neurologic features, and its neuroimaging correlates. Thus, the purpose of the current study was to describe the specific speech features, non-speech neurologic findings, and imaging findings for a relatively large series of patients presenting with PSD as the first and predominant sign of a presumed neurodegenerative disease.

Methods

This retrospective study was conducted with the approval of the Mayo Clinic Institutional Review Board.

Participants

Participants were identified through a database search of patients seen at Mayo Clinic Rochester, in the Division of Speech Pathology, between 2006 and 2012, with a communication disorder diagnosis of spastic dysarthria as the only or the predominant speech disorder and a null history of acute medical diagnoses to explain the dysarthria (e.g., stroke, traumatic brain injury). Inclusion criteria were: (1) Speech difficulties as the presenting or primary neurologic complaint; (2) Duration of symptoms at final follow-up of at least 6 months; (3) Speech diagnosis of spastic dysarthria (defined under Results) as the primary communication deficit; and (4) No evidence of speech or bulbar symptoms indicative of LMN involvement (i.e., flaccid dysarthria, atrophy, fasciculations), or neurological findings indicative of lower motor neuron involvement elsewhere.

A total of 25 patients (18 females) met inclusion and exclusion criteria. The mean age of onset of spastic dysarthria was 63.1 years (range 46 to 87 years); mean age of presentation 66.1 years (range 47 to 89 years); and mean duration of symptoms at final evaluation 30 months (range 6 – 84 months). All patients reported normal speech prior to onset of the presenting dysarthria.

MRI processing

All PSD patients completed head imaging with an MRI scan. Seven had a volumetric MRI performed with a standardized protocol(12) suitable for volumetric analysis. The mean age at scan of these patients was 65.4 years (range 50-74 years) and 57% were female. These patients were matched 1:2 by age and gender to a group of 14 healthy controls (mean age 65.4 years, range 50-74, 43% male).

All images underwent pre-processing correction for gradient non linearity(13) and intensity non-uniformity(14). Voxel-based morphometry (VBM)(15) (<http://www.fil.ion.ucl.ac.uk/spm>) in SPM5 characterized patterns of grey and white matter atrophy in PSD patients compared to controls. Briefly, all images were normalized to a customized template and segmented into grey matter, white matter and CSF using customized tissue probability maps and the unified segmentation routine(16) followed by the HMRF cleanup step. Grey and white matter images were modulated and smoothed at 8 mm full width at half maximum. A two-sample t-test was used to assess grey and white matter loss in PSD subjects compared to controls. Results were assessed for multiple comparisons using the false discovery rate (FDR)(17) at a statistical threshold of $p < 0.05$ and uncorrected at $p < 0.001$.

FDG-PET processing

Nine PSD patients, seven of whom also had MRI imaging, had 18F Flurodeoxyglucose positron emission tomography (FDG-PET) performed according to a standardized protocol(18). Fully automated three-dimensional stereotactic surface projections (SSP) was used for the interpretation of the FDG-PET. Scans were realigned and spatially normalized and underwent nonlinear warping. The scans were sampled at 16,000 predefined cortical locations and projected on a 3-dimensional image. The activity was normalized to the pons and compared with an age-segmented normative database, yielding a 3-dimensional SSP z score image. The image produced by this analysis produces a metabolic map using the z scores as calculated for each surface pixel(19). The software package used to perform this analysis was CortexID (GE Healthcare, Waukesha, Wisconsin).

Results

Speech

All patients demonstrated speech characteristics consistent with spastic dysarthria(1, 2) (Table 1). Although many abnormal speech characteristics may be present, the key distinguishing and defining features of spastic dysarthria typically include strained voice quality, slow speaking rate, monopitch and monoloudness, and slow and regular speech alternating motion rates (AMRs)(1). Strained voice quality and slow, regular speech AMRs were present in all patients. All but two patients additionally exhibited slow rate, monopitch and monoloudness, and imprecise articulation. More than half exhibited hypernasality, and approximately one-third exhibited short phrases. All of these features are compatible with spastic dysarthria.

Four patients (16%) also had concomitant motor speech disorders. One patient had ataxic dysarthria characterized by irregular articulatory breakdowns. Three had apraxia of speech (AOS), defined as a speech planning/programming disorder characterized by distorted

substitutions, vowel distortions, pronounced difficulty with multisyllabic words (e.g., increased errors with increasing length), segmentation of syllables within or between words, and/or intrusive neutral vowel in consonant clusters (e.g. "buhlend"/blend). In all cases, spastic dysarthria was the predominant speech disorder.

Nonspeech Neurologic findings

Nonspeech neurologic signs considered compatible with spastic dysarthria were observed during speech examination (Table 2). These included orofacial weakness, slow oral movements, reduced velar movement during vowel prolongation, reduced sharpness of cough and/or glottal coup, and pathologic oral reflexes (i.e., suck, snout, palmoventral, jaw jerk). Jaw clonus was occasionally evident. Drooling and/or dysphagia were common complaints. Approximately 40% of the patients had pseudobulbar affect.

Upper extremity weakness and/or spasticity resulting in slow AMRs were observed in over half of the patients. Lower limb spasticity and hyper-reflexia were present in approximately one-third of the patients; frank lower limb weakness was not reported. Half of the patients had asymmetric motor findings predominantly affecting the left side. Observed less frequently were a unilateral Hoffman sign and unilateral Babinski reflex. No patients had striking eye movement abnormalities. Eight patients had no abnormal neurological findings.

Electromyographic (EMG) assessment was conducted on 23 patients. No patients demonstrated evidence of diffuse motor neuron disease or met El Escorial criteria for ALS(20). One patient exhibited evidence of long-standing motor neuropathy without fasciculations or fibrillation potentials.

The neurologic diagnoses at the time of initial assessment were primary lateral sclerosis (PLS; n= 12), pseudobulbar palsy (n = 6; defined as a syndrome consisting of spastic dysarthria, dysphagia, pathologic oral reflexes and pseudobulbar affect), or progressive spastic dysarthria (n = 7).

Follow up evaluation

Ten patients were seen for one or more speech evaluations up to four years after the initial evaluation. Seven patients continued to display speech features consistent with those noted at the initial evaluation. One patient who had irregular articulatory breakdowns suggestive of ataxic dysarthria at the time of initial assessment was no longer exhibiting this feature at follow-up evaluation; the speech diagnosis changed from mixed spastic-ataxic to spastic dysarthria. One patient developed features suggestive of AOS, and another became anarthric. All patients demonstrated progression in severity of spastic dysarthria between the initial and subsequent speech evaluations.

Eight patients were seen for neurologic evaluation six months to four years after the initial diagnosis. The medical diagnoses were unchanged at the time of final evaluation. Dysarthria and other pseudobulbar symptoms remained the most prominent features of the disorder.

MRI results

The MRI findings were non-specific (e.g., white matter hyperintensities and non-focal volume loss due to aging), and without any identifiable lesions (e.g. tumors or strokes) to account for the clinical presentations. The subgroup of patients included in volumetric MRI and FEG-PET analyses were representative of the full cohort with respect to severity of PSD and nonspeech neurologic impairment. This subgroup had longer symptom duration at the time the scans were completed compared to the full cohort.

After correcting for multiple comparisons, the subgroup of seven PSD patients that underwent volumetric MRI showed bilateral patterns of white matter volume loss, but no regions of grey matter volume loss, when compared to controls (Figure 1). Regions of white matter volume loss were observed predominantly underlying the motor cortex (BA 4), including the frontoparietal operculum (BA 43), which appear to reflect involvement of the corticofugal projection fibers. White matter volume loss also extended anteriorly into premotor cortex and posterior prefrontal cortex, and was observed in the body of corpus callosum and anterior brainstem. Brainstem white matter loss particularly involved the middle third of the cerebral peduncle of the midbrain which reflects involvement of descending corticospinal and corticobulbar fibers. At the uncorrected threshold however we did observe grey matter loss affecting bilateral medial and lateral motor and premotor cortices.

FDG-PET

For the subgroup of nine patients who underwent FDG-PET, scans showed absent to subtle hypometabolism in the cortex (Figure 2). The majority of cases did not show focal abnormalities, although focal areas of hypometabolism affecting the premotor and motor cortices were observed in five patients (patients 10, 14, 18, 22 and 25; red arrows), four of whom had a time from onset to scan of longer than two years. Patterns of hypometabolism were bilateral in all patients, but greater in the right hemisphere in patients 14, 18 and 22.

Discussion

This study is the first to describe clinical and imaging features in a large cohort of patients with PSD. The findings were consistent with the classic description of spastic dysarthria with respect to predicted site of lesion, non-speech orofacial neurologic findings, and speech characteristics(2, 5). Darley, Aronson, and Brown(2) posited that the dysarthria associated with pseudobulbar palsy requires damage to bilateral corticobulbar pathways. Indeed, our MRI analysis revealed that PSD particularly targets the white matter, with degeneration observed beneath the motor cortex and mid cerebral peduncle, suggestive of involvement of descending corticospinal and corticobulbar fibers, bilaterally. Less striking grey matter loss and hypometabolism were also observed in the motor and premotor cortices.

The nonspeech oral movement characteristics associated with PSD(2) in our patients are consistent with those described for spastic dysarthria in general. These include reduction of force and speed on clinical measures of tongue, lip, and velar movements without evidence of atrophy; pathologic oral reflexes; and dysphagia. Neurological findings of an upper motor neuron pattern of weakness, spasticity, hyper-reflexia, unilateral Babinski and Hoffmann, and jaw clonus are consistent with imaging findings of motor cortex, corticospinal and corticobulbar tract involvement. Interestingly, pyramidal tract signs identified tended to be asymmetric and more prominent on left side, in keeping with greater volume loss in the right mid cerebral peduncle compared to the left mid cerebral peduncle.

Progressive spastic dysarthria may be the presenting symptom of motor neuron disease and may precede features of flaccid dysarthria (resulting in mixed spastic-flaccid dysarthria). The current sample demonstrates that spastic dysarthria, characterized by strained phonatory quality, slow rate, imprecise articulation, and slow, regular alternate motion rates may progress for an extended time without emergence of flaccid characteristics (e.g., phonatory flutter, prominent weakness, atrophy, and fasciculations). This mirrors the presentation of corticospinal symptoms in PLS. Descriptions of PLS suggest that bulbar symptoms rarely precede spinal symptoms(21–25). Moreover, reports describing progressive pseudobulbar syndromes have rarely characterized the nature of observed dysarthria, either with respect to the speech diagnosis (e.g., spastic dysarthria (23, 26, 27)) or specific speech features(24).

Patients with PLS with initial pseudobulbar symptoms typically ultimately develop limb symptoms(21–23, 25), but a small number do not(24, 26). Fourteen patients in the current study demonstrated limb involvement (3/8 with one year duration, 3/7 with 1<3 years duration, 8/9 with 3 or more years duration), even though dysarthria and other pseudobulbar symptoms remained the most prominent features of the disorder.

The patients in our study were initially diagnosed as PSD, pseudobulbar palsy or PLS. These are all appropriate terms given the clinical presentations. However, the most prominent symptom was progressive difficulty with speech and all patients were determined to have a spastic dysarthria. Patients with PLS(28) may present with bulbar symptoms including dysarthria and dysphagia, but the term PLS implies that there is limb involvement. Since some of our PSD patients had limb involvement initially, and others eventually developed limb involvement, it is our opinion that PSD could be considered a variant of, or a focal presentation of, PLS(29).

Conclusions

We have characterized a neurodegenerative condition that begins focally with spastic dysarthria and then spreads through a network (primarily motor) that may eventually affect speech praxis and limb movements, but in which the spastic dysarthria remains the most prominent deficit. This is not unlike other neurodegenerative conditions that may present as a focal language or speech deficit (e.g., primary progressive aphasia and/or primary progressive apraxia of speech) but ultimately evolve to include more widespread impairment of sensorimotor or cognitive functions. We propose that the term “progressive spastic dysarthria” best characterizes this pattern of deficit.

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Figure 1.

Three-dimensional renderings showing regions of white matter loss in a group of seven PSD patients compared to controls. An axial slice through the brainstem is also shown. Results are shown after correction for multiple comparisons using false discovery rate at $p < 0.05$.

Figure 2.

Three-dimensional stereotactic surface projections showing FDG-PET results for nine PSD patients. Patient numbers are shown on the left and time from onset to scan on the right. Red arrows highlight regions of premotor and motor hypometabolism.

Table 1

Demographic features, non-speech bulbar and non-bulbar neurologic findings

Patient	Sex	Age at onset	Duration of symptoms at final follow-up (years)	Non-speech bulbar neurological findings	Non-speech non-bulbar neurological findings	EMG findings
1	F	87	2	lip and tongue weakness, pseudobulbar affect, mild periorbital weakness, occasional dysphagia		normal
2	M	69	5	reduced range, strength, and speed of lip and tongue movements, mild right facial droop, minor dysphagia	right UMN pattern weakness, Hoffman sign on right	normal
3	F	62	4	mild tongue weakness and slowness, subtle nonverbal oral apraxia, pseudobulbar affect	bilateral (right > left) upper extremity spasticity with slow AMRs	normal
4	M	57	1	pseudobulbar affect, drooling, dysphagia		normal
5	F	79	2	right lower face and tongue weakness, dysphagia	UMN limb weakness	normal
6	F	46	3.5	tongue weakness, brisk jaw jerk		normal
7	F	79	3	drooling, dysphagia, mild lip weakness	mild left upper extremity spasticity with slow AMRs	normal
8	F	63	1	mild lower facial weakness		normal
9	F	74	3	dysphagia, drooling, facial and tongue weakness, neck flexor weakness	spasticity left>right leg	normal
10	M	58	7	equivocal nonverbal oral apraxia	spastic paraparesis and left upper extremity spasticity, left Babinski; mild postural/kinetic tremor	evidence for longstanding motor neuropathy or neuropathy without fasciculation or fibrillation potential
11	F	60	3	dysphagia, pseudobulbar affect, nonverbal oral apraxia	mildly brisk, symmetric reflexes and decreased limb AMRs	normal
12	M	46	1	dysphagia, tongue weakness and slowness, bifacial weakness	left side UMN type weakness, left Babinski	normal
13	F	72	1	dysphagia, pseudobulbar affect, mild tongue and lower facial weakness	brisk (non-pathologic) reflexes, mild slow limb AMRs	normal
14	F	66	5	dysphagia, drooling, minimal jaw opening, mild left facial weakness	left upper extremity spasticity with slow AMRs; 2-3 beat left ankle clonus;	normal
15	M	63	1	dysphagia, pseudobulbar affect, tongue and facial weakness	mild left upper extremity UMN weakness	normal
16	M	48	2	minor dysphagia, drooling, brisk jaw, jerk, jaw clonus, pseudobulbar affect, tongue weakness		normal
17	F	56	1	minor dysphagia, tongue and lip weakness, positive suck and snout reflexes		normal

Patient	Sex	Age at onset	Duration of symptoms at final follow-up (years)	Non-speech bulbar neurological findings	Non-speech non-bulbar neurological findings	EMG findings
18	M	71	2	pseudobulbar affect, nonverbal oral apraxia		normal
19	F	50	2	dysphagia, pseudobulbar affect, tongue weakness, brisk jaw jerk reflex	mild hyperreflexia in upper and lower extremities (not pathologic)	normal
20	F	63	2	dysphagia, pseudobulbar affect, jaw clonus, reduced tongue strength and speed	left upper and lower extremity spasticity with slow AMRs; spastic/apraxic gait	normal
21	F	66	1	dysphagia, subtle jaw clonus, mild tongue weakness, brisk jaw jerk reflex	mild hyperreflexia in upper and lower extremities (not pathologic)	normal
22	M	56	6	drooling, minor dysphagia, pseudobulbar affect, jaw clonus	left UMN pattern weakness, bilateral limb spasticity (left > right), spastic gait circumducting left leg; subtle left Babinski	n/a
23	M	62	1.5	dysphagia, pseudobulbar affect, facial, tongue, and velar weakness	frontal release signs, hyper-reflexia, reduced right arm swing, unsustained clonus at both ankles	n/a
24	F	55	1	minor dysphagia, jaw and tongue weakness		normal
25	F	70	1	dysphagia, pseudobulbar affect, tongue and palatal weakness		normal

n/a: not administered

Table 2

Motor speech characteristics

Patient	Intelligibility Impairment	Strained Voice Quality	Slow rate	Monopitch-Monoloudness	Hypernasality	Articulatory Imprecision	Slow Regular AMRS	Other
1	moderate	marked		marked	marked-severe	marked	marked	short phrases
2	marked	marked	marked	mild	mild	moderate	mild	reduced loudness
3	mild	moderate-marked	marked	marked		mild-moderate	marked	excess equal stress, reduced loudness
4	normal	mild	mild	mild-moderate	minimal	minimal	moderate	
5	moderate	marked	marked	marked-severe	mild-moderate	marked-severe	moderate-marked	short phrases
6	mild	mild-moderate	moderate	mild		mild-moderate	mild	
7	normal	moderate	mild-moderate	moderate		moderate	mild	reduced loudness
8	mild	moderate	mild-moderate	mild-moderate		mild	mild	irregular articulatory breakdown
9	mild-moderate	moderate-marked	moderate	moderate	mild	mild-moderate	moderate	apraxia of speech
10	normal	minimal	moderate	moderate	mild-moderate	mild	moderate	excess, equal stress, apraxia of speech
11	marked	marked	marked-severe	marked		marked	marked	apraxia of speech
12	normal	mild	mild	mild		mild	mild-moderate	
13	mild	marked-severe	marked	marked		minimal	marked	
14	severe	marked-severe	severe	severe		severe	mild-moderate	
15	mild	moderate	mild	moderate	moderate	mild-moderate	moderate	
16	normal	minimal	mild-moderate	moderate	mild-moderate		moderate	excess, equal stress
17	moderate	marked		marked	marked	marked	marked	
18	severe	marked	severe	severe		severe	moderate-marked	
19	mild	mild	minimal		minimal	mild-moderate	mild	
20	moderate	marked-severe	severe	marked-severe	marked-severe	marked	marked	
21	normal	moderate	mild-moderate	mild-moderate	mild	mild	moderate-marked	
22	normal	moderate	moderate	moderate	mild-moderate	minimal	mild-moderate	
23	severe	marked-severe	marked-severe	severe	marked-severe	severe	marked-severe	
24	mild	moderate	mild			mild	mild	reduced loudness
25	moderate	moderate	moderate-marked	marked	marked-severe	moderate-marked	moderate	