

The Efficacy of Acoustic-Based Articulatory Phenotyping for Characterizing and Classifying Four Divergent Neurodegenerative Diseases Using Sequential Motion Rates

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ABSTRACT

Despite the impacts of neurodegeneration on speech function, little is known about how to comprehensively characterize the resulting speech abnormalities using a set of objective measures. Quantitative phenotyping of speech motor impairments may have important implications for identifying clinical syndromes and their underlying etiologies, monitoring disease progression over time, and improving treatment efficacy. The goal of this research was to investigate the validity and classification accuracy of comprehensive acoustic-based articulatory phenotypes in speakers with distinct neurodegenerative diseases. Articulatory phenotypes were characterized based on acoustic features that were selected to represent five components of motor performance: *Coordination*, *Consistency*, *Speed*, *Precision*, and *Rate*. The phenotypes were first used to characterize the articulatory abnormalities across four progressive neurologic diseases known to have divergent speech motor deficits: amyotrophic lateral sclerosis (ALS), progressive ataxia (PA), Parkinson's disease (PD), and the nonfluent variant of primary progressive aphasia and progressive apraxia of speech (nfPPA+PAOS). We then examined the efficacy of articulatory phenotyping for disease classification. Acoustic analyses were conducted on audio recordings of 217 participants (i.e., 46 ALS, 52 PA, 60 PD, 20 nfPPA+PAOS, and 39 controls) during a sequential speech task. Results revealed evidence of distinct articulatory phenotypes for the four clinical groups and that the phenotypes demonstrated strong classification accuracy for all groups except ALS. Our results highlight the phenotypic variability present across neurodegenerative diseases, which, in turn, may inform (1) the differential diagnosis of neurological diseases and (2) the development of sensitive outcome measures for monitoring disease progression or assessing treatment efficacy.

Keywords: neurodegenerative disease; differential diagnosis; acoustic analyses; articulatory features; domain knowledge

INTRODUCTION

Neurodegenerative diseases affect millions worldwide and often result in debilitating speech deficits (Batista & Pereira, 2016; Hartelius et al., 2008). Over the past two decades, researchers have been characterizing the varied presentations of speech impairment across different neurodegenerative diseases—an effort referred to as *speech phenotyping* (Kent & Kim, 2003b; Lansford et al., 2014; Poole et al., 2017; Rusz et al., 2011, 2018; Schalling & Hartelius, 2004; Skodda, Visser, et al., 2011; Tsuboi et al., 2015; Utianski et al., 2018; Vogel et al., 2017). The comprehensive phenotyping of behaviors, such as speech, is of broad interest to the clinical neurology community for its potential to inform (1) the differential diagnosis of neurological diseases and (2) the development of sensitive outcome measures for monitoring disease progression or assessing treatment efficacy (Miravittles et al., 2012; Titova & Chaudhuri, 2017). The purpose of this study was to characterize the articulatory phenotypes of four divergent neurodegenerative conditions and determine the potential utility of these phenotypes for informing disease classification.

The Need for Quantitative Measures of Speech

Speech abnormalities are often one of the earliest signs of disease onset (Duffy, 2013). Yet, while the oral motor exam is a key part of the neurological assessment, specific *speech* impairments (e.g., uncoordinated articulatory movements, inconsistent syllable productions) are less routinely relied upon in the diagnostic process. The underutilization of speech in the neurology clinic may be, in part, due to the lack of a quantitative, clinically meaningful method for characterizing speech abnormalities. One of the most established paradigms for characterizing speech motor impairments was developed by Darley, Aronson, and Brown (DAB) over five decades ago (Darley et al., 1969a, 1969b). For the articulatory subsystem, speech-language pathologists are instructed to rate speakers on several auditory-perceptual dimensions, such as "imprecise consonants," "distorted vowels," or "irregular articulatory breakdowns." This paradigm has been widely adopted by speech clinicians and has highlighted the heterogeneity of speech impairments across neurologic populations. However, the subjectivity of this approach has raised questions regarding its accuracy and reliability (Borrie et al., 2012; Kent, 1996; Zyski & Weisiger, 1987). Researchers have, therefore, been exploring the utility of objective, instrumental-based measures of speech (Green et al., 2013). Acoustic analyses are one of the most rapidly developing speech analytic techniques because they are widely available, non-invasive, efficient, and affordable.

The Potential Clinical Utility of Measures of Articulatory Function

Articulatory motor function is of particular interest for informing both disease classification and sensitive outcome measures. From a diagnostic perspective, articulatory abnormalities manifest in unique motor symptoms (e.g., irregular articulatory breakdowns) that correspond with underlying neuropathologies of different movement disorders (e.g., cerebellar degeneration) (Ackermann, 2008; Darley et al., 1969b, 1969a; Hirose, 1986; Kent et al., 1979; Poole et al., 2017; Spencer & Slocumb, 2007). Importantly, when examining the speech of speakers with neurodegenerative diseases, identifying features that are spared is arguably as important as identifying those that are impaired. For example, slow rate and imprecision are sensitive markers of both ALS and progressive ataxia (PA) (Duffy, 2020), but irregular articulatory breakdowns are specific to PA (Duffy, 2020), as speakers with ALS have been shown to exhibit less articulatory variability than control speakers (Mefferd et al., 2014). Similarly, although a slow rate of speech is present in most dysarthria subtypes (Duffy, 2020), preserved or even increased rate has been reported in speakers with PD (Blanchet & Snyder, 2009; Kim et al., 2009; Rowe et al., 2020). These findings and others provide the rationale for further investigation into the efficacy of articulatory features as indicators of different movement disorders (Cordella et al., 2017; Green et al., 2013; Orozco-Arroyave et al., 2016; Shellikeri et al., 2016; Takakura et al., 2019). Moreover, articulatory impairments are strongly associated with speech intelligibility (De Bodt et al., 2002; Kent et al., 1989;

Lee et al., 2014; Rong et al., 2015; Turner et al., 1995; Weismer et al., 2001) and have been shown to be highly sensitive to changes in disease status (Rong et al., 2015). Indeed, the growing focus on articulatory features has yielded studies demonstrating the potential for acoustic-based articulatory features to improve early disease detection (Allison et al., 2017) and serve as a useful tool for monitoring disease progression or assessing the efficacy of behavioral or pharmaceutical treatments (Green et al., 2018).

A Framework for Comprehensively Characterizing Articulatory Motor Impairments

Although the classification of speech motor disorders is more accurate when based on multiple speech features rather than individual features (Ballard et al., 2016; Basilakos et al., 2017), there is currently no established set of measures that can comprehensively characterize articulatory function (Green et al., 2013). Over the past several decades, articulation has been described using a wide variety of labels (e.g., "distinctiveness," "imprecision," "coupling," "coarticulation"). The vast number of dimensions and lack of conceptual frameworks have led to challenges with interpreting measures and defining the constructs that might be most important for treatment or differential diagnosis (Berisha et al., 2021; Miller, 1992). Our recent work has thus sought to develop and validate a unifying framework for profiling the diversity of articulatory motor abnormalities described in the extant speech motor literature. The framework characterizes articulatory function using five key components of motor control (Rowe et al., 2020, 2021; Rowe & Green, 2019): *Coordination*, *Consistency*, *Speed*, *Precision*, and *Rate*. The goal of this framework is to provide a simple, comprehensive, and testable scheme that can allow for comparisons of articulatory function across clinical populations with divergent deficits.

Acoustic Correlates of Articulatory Impairments in Different Neurodegenerative Diseases

Throughout the past several decades, the articulatory patterns of many neurodegenerative diseases have been characterized using acoustic-based articulatory features. While the majority of acoustic studies have focused on disease detection (i.e., distinguishing individuals with a disease from healthy controls) (Mei et al., 2021), a subset of studies investigated articulatory differences across multiple clinical groups (see Table 1, which uses our framework as an organization scheme). To date, most studies have focused on distinguishing speakers with PD from speakers with other diseases. The most consistent findings are that speakers with PD exhibit (1) *greater impairments in Precision* compared to speakers with multiple sclerosis (MS) (Kuo & Tjaden, 2016), Huntington's disease (HD) (Ackermann et al., 1995), early stage or mild ALS (Mefferd, 2015; Rowe et al., 2020), and PA (Ackermann et al., 1995); (2) *less impaired repetition Rate* compared to speakers with PA (Ziegler, 2002), late stage ALS (Rowe et al., 2020), cerebellar variant of multiple systems atrophy (MSA-C) (Rusz et al., 2019), and MS (Tjaden & Watling, 2003); (3) *less impaired Coordination* compared to speakers with early ALS (Rowe et al., 2020), MSA (Daoudi et al., 2021; Rusz et al., 2019; Tykalova et al., 2017), and progressive supranuclear palsy (PSP) (Tykalova et al., 2017); and (4) *less impaired Consistency* compared to speakers with MSA (Rusz et al., 2015), PSP (Skodda et al., 2012), HD (Ackermann et al., 1995), and MS (Tjaden & Watling, 2003). Although these findings provide important information regarding how diseases differ on specific articulatory features, this research is limited in the diversity of populations and articulatory characteristics examined in one study. Indeed, Ziegler (2002) investigated three divergent populations (i.e., PA, PD, and AOS) but primarily examined articulatory Rate (Ziegler, 2002). Similarly, Rusz and colleagues examined measures of Coordination, Consistency, Precision, and Rate but only in populations with atypical parkinsonian syndromes (APS) (i.e., MSA, PD, and PSP) (Rusz et al., 2015). No study, to our knowledge, has examined a wide range of both neurological/ pathophysiological deficits *and* articulatory characteristics, which is crucial for modeling and comparing the diversity of articulatory deficits across disease types.

Table 1. Findings from current literature on distinguishing neurodegenerative populations using acoustic-based articulatory features (< indicates poorer performance on that measure).

	ALS	AOS	APS	HD	MS	PA	PD
ALS							

AOS	NA					
APS	NA	NA				
HD	NA	NA	NA			
MS	NA	NA	NA	NA		
PA	NA	Consistency <i>syllable variability:</i> PA = AOS [1]	NA	Consistency <i>syllable variability:</i> PA > HD [2]	NA	
		Repetition Rate <i>alternating motion rate:</i> PA < AOS [1]		Precision <i>incomplete closure:</i> PA < HD [2]		
PD	Coordination <i>voice onset time:</i> ePD > eALS [3] IPD = lALS [3]	Consistency <i>syllable variability:</i> PD = AOS [1]	Coordination <i>devoicing of plosives and fricatives:</i> PD > MSA [13]	Consistency <i>syllable variability:</i> PD > HD [2]	Coordination <i>stop gap duration:</i> PD > MS [11]	Consistency <i>syllable variability:</i> PD = PA [1,2]
	Consistency <i>voice onset time variability:</i> ePD = eALS [3] IPD = lALS [3]	Repetition Rate <i>alternating motion rate:</i> PD = AOS [1]	<i>voice onset time:</i> PD = MSA-C [6] PD > MSA-P [6]	Precision <i>incomplete closure:</i> PD < HD [2]	Consistency <i>syllable variability:</i> PD > MS [11]	Precision <i>incomplete closure:</i> PD < PA [2]
	Speed <i>second formant slope:</i> ePD < eALS [3] IPD > lALS [3]		<i>voice onset time (voiced):</i> PD > MSA [7] PD = PSP [7]		Precision <i>second formant interquartile range:</i> PD < MS [12]	Repetition Rate <i>alternating motion rate:</i> PD > PA [1]
	Precision <i>second formant slope variability:</i> ePD = eALS [3] IPD > lALS [3]		<i>voice onset time (voiceless):</i> PD > MSA [7] PD > PSP [7]		Repetition Rate <i>alternating motion rate:</i> PD > MS [11]	
	<i>vowel space area:</i> PD = ALS [4]		Consistency <i>syllable variability:</i> PD > MSA [8] PD > MSA-C [8] PD = MSA-P [8] PD > PSP [8,9]		<i>sequential motion rate:</i> PD > MS [11]	
	<i>vowel dispersion:</i> PD < ALS [5]		Precision <i>resonant frequency attenuation:</i> PD = MSA-C [8] PD = MSA-P [8]			
	Repetition Rate <i>sequential motion rate:</i> ePD = eALS [3] IPD > lALS [3]		<i>vowel area index:</i> PD = MSA [8] PD > PSP [8] PD > PSP [10]			
			Repetition Rate <i>alternating motion rate:</i> PD = MSA [9] PD = PSP [9,10]			
			<i>sequential motion rate:</i> PD > MSA-C [7] PD = MSA-P [7]			

Note. AOS = apraxia of speech; ALS = amyotrophic lateral sclerosis (e = early, l = late); APS = atypical parkinsonian syndrome; HD = Huntington's disease; MS = multiple sclerosis; MSA = multiple systems atrophy; MSA-C = cerebellar variant of MSA;

MSA-P = parkinsonian variant of MSA; PA = progressive ataxia; PD = Parkinson's disease (e = early, l = late); PSP = progressive supranuclear palsy; [1] Ziegler, 2002; [2] Ackermann et al., 1995; [3] Rowe et al., 2020; [4] Weismer et al., 2001; [5] Mefferd, 2015; [6] Rusz et al., 2019; [7] Tykalova et al., 2017; [8] Rusz et al., 2015; [9] Skodda et al., 2012; [10] Skodda et al., 2011; [11] Tjaden & Watling, 2003; [12] Kuo & Tjaden, 2016; [13] Daoudi et al., 2021. AOS refers to acquired AOS rather than neurodegenerative, the latter of which is referred to as progressive AOS (PAOS).

Current Study

In the current study, we used our acoustic-based framework to comprehensively characterize articulatory motor abnormalities in four populations with divergent neurodegenerative diseases. We then assessed the efficacy of articulatory phenotyping for disease classification. Importantly, our intention is not to use speech as the sole indicator of disease, but rather to explore the limits of the information speech can provide for *informing* the complex process of neurologic diagnosis. We examined ALS, which involves upper and lower motor neuron degeneration; PA, which involves cerebellar circuit degeneration; PD, which involves basal ganglia circuit degeneration; and the nonfluent variant of primary progressive aphasia and progressive apraxia of speech (nfPPA+PAOS), which involves left frontal lobe degeneration. The clinical groups were chosen to represent a wide diversity of neurological abnormalities and pathophysiologies that reflect and extend the clinico-anatomic model of Darley and colleagues (Darley et al., 1969a, 1969b; Duffy, 2020; Kent et al., 2000) (see Figure 1). Our research objectives and questions were as follows:

1. *To characterize the articulatory phenotypes of four divergent neurodegenerative diseases.*
 - a. What are the articulatory phenotypes of neurodegenerative diseases known to have divergent speech motor deficits?
 - b. Do the acoustic features measure distinct constructs and, therefore, provide unique information about articulatory function for each neurodegenerative disease?
2. *To determine the accuracy of neurodegenerative disease classification based on articulatory phenotypes.*
 - a. What is the efficacy of articulatory phenotypes for classifying divergent neurodegenerative diseases?
 - b. Is a profile of articulatory features more diagnostically useful than individual features for neurodegenerative diseases?

MATERIALS AND METHODS

Participants

Data from the four groups of speakers with neurodegenerative diseases (N = 46 for ALS, 52 for PA, 60 for PD, and 20 for nfPPA+PAOS) and neurotypical controls (N = 39) were obtained from several different extant databases (see Table 2). The participants in the four clinical groups presented with either dysarthria (i.e., ALS, PA, and PD) or AOS (nfPPA+PAOS), as determined by two speech-language pathologists, and demonstrated a mild speech impairment on average. The presence of AOS was based on established criteria as operationalized previously by Cordella and colleagues (Cordella et al., 2019). These criteria were adapted from the Apraxia of Speech Rating Scale (ASRS), which is a validated clinical indicator of AOS among individuals with nfPPA and PAOS (Strand et al., 2014), and were evaluated during AOS-specific tasks (e.g., multisyllable word repetition) and spontaneous speech to make a holistic assessment of AOS.

All participants were native English speakers, had normal hearing and vision, and had no cognitive impairments that may have interfered with the ability to follow directions. Control participants also had no history of speech, language, or neurological impairments. Information regarding the specific screening protocols for hearing and cognition was not available for all databases. However, standardized hearing screenings were performed for the XRMB dataset and at the MGH ALS Clinic, and cognitive screenings were conducted with the ALS Cognitive Behavior Screen (Woolley et al., 2010) at the MGH ALS Clinic and with the Standardized Mini-Mental State Examination (Molloy & Clarnette, 1999) at the University of Buffalo.

All neurological diagnoses were based on clinical evaluations by neurologists who specialized in each respective disease. The diagnosis of ALS was based on El Escorial criteria (Brooks et al., 2000); PA was used as an umbrella term to encompass speakers with Friedreich’s ataxia (FA) and cerebellar/spinocerebellar ataxia, whose diagnoses were confirmed with genetic testing (Klockgether et al., 2019; Pandolfo, 2008); the diagnosis of PD was based on criteria developed by the International Parkinson and Movement Disorder Society (MDS) (Postuma et al., 2015); lastly, the diagnosis of PPA was based on Mesulam’s guidelines and a prominent, isolated language deficit (Mesulam, 2001), and the classification of the nonfluent variant was based on criteria outlined by Gorno-Tempini and colleagues (Gorno-Tempini et al., 2011).

Diagnosis	Speech Motor Subtype	Neurological Deficit	Pathophysiological Impairment	Example Articulatory Patterns
ALS	spastic, flaccid, or mixed spastic-flaccid dysarthria	upper and/or lower motor neurons	strength and/or tone	reduced speed distorted vowels
PA	ataxic dysarthria	cerebellum	timing	uncoordinated syllable sequences irregular breakdowns
PD	hypokinetic dysarthria	basal ganglia	scale and speed	short rushes of speech repeated phonemes
nfPPA+PAOS	apraxia	left frontal lobe	planning	slow rate segmented syllables

Figure 1. The clinical groups selected for this study along with their associated speech motor subtype, presumed neurological deficit and pathophysiological mechanism, and example articulatory patterns based on the Darley, Aronson, and Brown (DAB) model (ALS = amyotrophic lateral sclerosis; PA = progressive ataxia; PD = Parkinson’s disease; nfPPA+PAOS = the nonfluent variant of primary progressive aphasia and progressive apraxia of speech).

Table 2. Demographic data, dataset, and speech characteristics of each speaker group.

Group	N	Datasets	Mean Age	Percent Female	Categorical Severity 1 (Normal) to 5 (Profound)	Continuous Severity 0 (Normal) to 100 (Profoundly Impaired)
ALS	46	25 from Beiwe dataset* 18 from MGH ALS Clinic 3 from XRMB dataset	55.26 (10.01)	40%	1.99 (.51)	19.28 (15.25)
PA	52	28 from NYU 15 from U of Washington 9 from U of Strathclyde	46.12 (17.10)	48%	1.87 (.49)	19.35 (13.54)
PD	60	42 from U of Buffalo 18 from XRMB dataset	64.60 (10.63)	37%	1.65 (.40)	10.08 (8.70)
nfPPA+PAOS	20	20 from MGH FTD Unit	70.50 (7.81)	59%	1.98 (.75)	19.61 (18.67)
Controls	39	23 from XRMB dataset 10 from MGH 6 from Beiwe dataset*	59.97 (9.50)	49%	1.53 (.42)	8.44 (7.34)

Note. ALS = amyotrophic lateral sclerosis; MGH FTD = Massachusetts General Hospital Frontotemporal Disorders; NYU = New York University; PA = progressive ataxia; PD = Parkinson’s disease; nfPPA+PAOS = the nonfluent variant of primary progressive aphasia and progressive apraxia of speech; XRMB = X-Ray Microbeam Speech Production Database (Westbury, 1994); * = collected remotely through cell phone recordings.

Data Collection

Acoustic data were collected from all participants during the sequential motion rate (SMR) task, in which they were instructed to repeat /pataka/ as quickly and accurately as possible on one breath. Data were compiled using several methods, including remote collection, which are denoted in Table 2. All data

were collected at a range of sampling frequencies between 16000 and 44100 Hz, which is sufficient for the analyses in this study (Kent et al., 2002). All recordings were screened for audio quality to ensure there was no environmental or signal noise during the speech sample. The in-person data was collected using professional quality microphones (e.g., AKG C410, Shure SM81 Condenser, Olympus VN-702PC digital recorder). The remote data was collected on mobile phones using the Beiwe application, an open-source software designed for Android and iOS devices that records using uncompressed, lossless formats (Berry et al., 2019). Speakers in the Beiwe dataset were instructed to record their speech samples in quiet environments. The feasibility of the Beiwe platform for detecting and tracking speech abnormalities in speakers with ALS has been previously demonstrated (Berry et al., 2019). Other recent work has similarly supported the use of remote data collection for speech telehealth and research given its strong reliability (Pierce et al., 2021) and accessibility (Schneider et al., 2021; Sevitz et al., 2021). Furthermore, a study comparing acoustic measures extracted from cell phone recordings and those extracted from professional recording devices revealed few differences between the two (Zhang et al., 2021). Nonetheless, the literature base examining the potential effects of remote data collection is new and, therefore, still inconclusive. Indeed, another study found that remote data collection may impact certain spectral (e.g., second formant slope, which we used to calculate our measures of Speed and Precision) and durational (e.g., voice onset time, which we used to calculate our measure of Consistency) measures (Ge et al., 2021). Thus, for the current study, we conducted statistical analyses to test for the potential effects of remote data collection on the second formant slope and voice onset time. Still, it should be noted that remote data collection may introduce other spectral and noise distortions that are not captured in this sole analysis.

Task Selection

The diadochokinetic (DDK) task (Fletcher, 1972), composed of the SMR task and alternating motion rate (AMR) task, is one of the few widely implemented, objective assessments for evaluating articulatory function in the clinic (Duffy, 2020). The SMR and AMR tasks involve repeating a syllable sequence (i.e., /pataka/) or single syllables (i.e., /pa/, /ta/, /ka/), respectively, as quickly and accurately as possible on one breath. Although the DDK task does not reflect functional communication (e.g., connected speech), prior work has demonstrated that DDK performance is a leading indicator of impending decreases in speaking rate (Nishio & Niimi, 2006; Rong et al., 2015) and that it is associated with other functional measures of speech, such as intelligibility (Becker et al., 2017; Samlan & Weismer, 1995). Moreover, the task assesses a speaker's ability to produce rapid muscle contractions of target articulators (e.g., lips, jaw, tongue), which challenges the motor system while imposing a relatively low burden on cognitive and linguistic functions. As a result, the DDK task been found to be an informative tool for distinguishing between speech motor disorders (Kent et al., 2022; Sidtis et al., 2011; Tjaden & Watling, 2003; Ziegler & Wessel, 1996). The SMR task, in particular, has strong diagnostic utility because it requires the ability to rapidly *transition* between movements, which is characteristically difficult for speakers with motor planning deficits (McNeil et al., 1995). Speakers with AOS often perform adequately on the AMR task but tend to exhibit variable error patterns on multisyllabic sequences in the SMR task (Duffy et al., 2014). Overall, the motoric demands this task imposes on speakers, particularly on those with vulnerable oral motor systems, could expose granular changes in articulatory function that may be diagnostically informative (Rong, 2020; Wang et al., 2009).

Severity Confound

Speech impairment severity is a common confound when attempting to categorize speech motor populations, as significant imbalances in severity could drive group classification (Kim et al., 2011). Including only speakers within a certain level allows us to determine the true discriminatory power of the acoustic features, which increases confidence that severity differences are not the primary driver of phenotype differences. To control for severity, we excluded speakers who had an articulatory severity of "Severe" or "Profound" based on the SMR task. For the severity ratings, two licensed speech-language pathologists with clinical expertise in speech motor disorders rated each speaker's level of articulatory

severity on a categorical scale of "Normal", "Mild", "Moderate", "Severe", or "Profound" (King et al., 2012). The clinicians were blind to speaker identity and diagnosis and were allowed to listen to the recordings as many times as needed. While the categorical ratings were used to stratify the speakers, the clinicians were also asked to rate each speaker on a 100-point visual analogue scale with endpoints labeled "No Impairment" (0) on the left and "Profound Impairment" (100) on the right. This method, which is consistent with procedures used in prior studies (Awan et al., 2009; Rowe et al., 2021), provides information about potential fine-grained differences in speaker severity. Lastly, in addition to excluding speakers who were identified as "Severe" or "Profound", we investigated the presence of statistically significant differences in both categorical and continuous severity ratings. A randomly selected 10% of the recordings were repeated for intrarater reliability (which was good to excellent for both severity ratings). Given our large sample size of 217, we felt 10% was an appropriate number of samples to assess for reliability, which also aligns with prior work (Tjaden et al., 2013). Interrater reliability (which was also good to excellent for both severity ratings) was assessed using 100% of the recordings since all recordings were rated by both clinicians.

Acoustic Analysis

The acoustic recordings were analyzed using Praat (Boersma, 2014). For the analysis, formant settings were set to a maximum frequency of 5500 Hz for women and 5000 Hz for men. Of the acoustic recordings from the clinical populations, 16 files (8%) were not able to be analyzed due to formant mistracking (5 [8%] from the ALS group, 4 [7%] from the PA group, 12 [17%] from the PD group, and 4 [15%] from the nfPPA+PAOS group). Each spectrogram from the remaining acoustic recordings was parsed for the first three repetitions of the sequence /pataka/ in which formant tracking was the most valid. For most participants, this was the second or third set of three repetitions. Formant tracking was empirically validated through visual inspection, which ensured robust formant tracking across the entire three repetitions with minimal deviation from the resonant band. Selecting well-defined repetitions from the front end of the speech sample allowed for more experimental control, as later repetitions may be influenced by factors such as fatigue or respiratory capacity. We selected only three repetitions because we sought to develop a brief protocol that could be used across speakers with a range of severities (e.g., speakers who are unable to produce more than three repetitions).

The first author and a trained research assistant segmented all of the SMR samples. To obtain interrater reliability (which was good to excellent for all five acoustic measures), the trained research assistant then re-measured the boundaries of 10% of the samples that the first author measured. To obtain intrarater reliability (which was also good to excellent for all five acoustic measures), the first author re-measured the boundaries of 10% of the samples she originally measured. The data required for each feature was extracted using a custom Praat script (Boersma, 2014), and the features were subsequently calculated using custom MATLAB (MathWorks, 2019) and R scripts (R Core Team, 2014). See Table 3 for the definition of each component and the methods used to calculate each corresponding acoustic feature. Figure 2 illustrates the portions of the spectrogram and waveform from which the five features were extracted.

Coordination (GapSyllProp): Coordination is arguably one of the most difficult articulatory constructs to capture acoustically. Based on the DAB paradigm and converging evidence from the speech literature, we expect to see the greatest Coordination deficits in speakers with PA and nfPPA+PAOS (Darley et al., 1969a, 1969b; Ogar et al., 2005; Spencer & France, 2016). Previous work has examined gap duration during DDK tasks as an indicator of coordinative or timing difficulties in populations with ataxia (Ozawa et al., 2001; Schalling et al., 2007; Schalling & Hartelius, 2004). Similarly, recent studies have documented segmented syllable repetitions in speakers with AOS/PAOS (Bouvier et al., 2021; Deger & Ziegler, 2002; Duffy, 2006; Kent & Rosenbek, 1983; Melle & Gallego, 2012; Staiger & Ziegler, 2008; Takakura et al., 2019). While pausing can indicate a linguistic or cognitive deficit in spontaneous speech (Rochester, 1973), intersyllabic pausing during a non-speech syllable repetition task, such as the DDK, can indicate difficulty with motorically planning or executing an utterance (Oytam et al., 2005). In the current

study, our measure of Coordination was the *relative duration of the silence between two articulatory gestures during each syllable transition* (e.g., /pa1/ to /ta1/, /ta1/ to /ka1/, or /ka1/ to /pa2/). In typical speakers, these transitions should be completed with little to no silence, whereas an abnormally prolonged stop gap relative to syllable length may indicate difficulty sequencing the closing and release gestures produced for the different stop consonants. Overall, this measure reflects the ability to transition smoothly between articulatory gestures—a key underlying construct of Coordination (Caruso et al., 1988; Gracco & Abbs, 1986). We used the *proportion of gap duration to syllable length* to control for potential confounding effects of rate. Furthermore, a proportion provides more information than absolute gap duration because it allows us to determine the *relative* difficulty of transitioning between sounds relative to the difficulty producing sounds. The measure is intended to be able to distinguish between a speaker who is slow overall (e.g., they produce equally long syllables and gaps) from a speaker who has difficulty with syllable transitions (e.g., they produce a markedly longer gap), the latter of which may be more indicative of a coordinative deficit.

Consistency (RepVarVOT): For our measure of Consistency, we used the *across-repetition variability in voice onset time* given its sensitivity to populations that lack stability in repeated sound productions (Hertrich & Ackermann, 1994; Kent et al., 1997; Kent & Rosenbek, 1983; McNeil et al., 1995; Rong, 2020; Rowe & Green, 2019). While variability in syllable length is another measure frequently used to index inconsistency (Ackermann et al., 1995; Rong, 2020; Ziegler, 2002), variability in VOT may be more sensitive than syllable length to smaller across-repetition alterations in the speech signal (Kent et al., 1997).

Speed (F2Slope): For our measure of Speed, we used the *second formant slope in the consonant transition of /k/* because previous research has demonstrated that the second formant slope is strongly associated with articulatory movement speed (Kent & Kim, 2003a; Kim et al., 2009; Yunusova et al., 2012). In light of prior work suggesting that formant slope is best calculated using stimuli that result in large changes in vocal tract configuration (Kim et al., 2009), /k/ was used in this study due to its robust transition.

Precision (ConVarF2Slope): For our measure of Precision, we used the *across-consonant variability in second formant slope in the consonant transitions of /p/, /t/, and /k/* given previous work demonstrating the utility of second formant slope (i.e., frequency range divided by time) as a cue for place and manner of articulation (Chen & Alwan, 2000; Delattre et al., 1955). The frequency range in second formant transitions depends on vocal tract length (e.g., bilabials tend to produce lower frequency ranges than alveolars) (MacKay, 2014), and the transition time depends on the rate of vocal tract constriction (e.g., plosives tend to produce more abrupt transition rates than fricatives) (Delattre et al., 1960). Thus, large differences between the transition slopes of three distinct consonants would indicate greater distinctiveness. This measure is relatively novel measure but was recently validated against kinematic and perceptual measures of Precision, revealing significant correlations of .72 and .68, respectively (Rowe et al., 2021).

Rate (RepRate): Lastly, for our measure of repetition Rate, we used the *number of syllables produced per second during the SMR task* because this measure has been shown to be highly sensitive to articulatory decline in speech motor populations (Nishio & Niimi, 2006; Tjaden & Watling, 2003; Ziegler & Wessel, 1996).

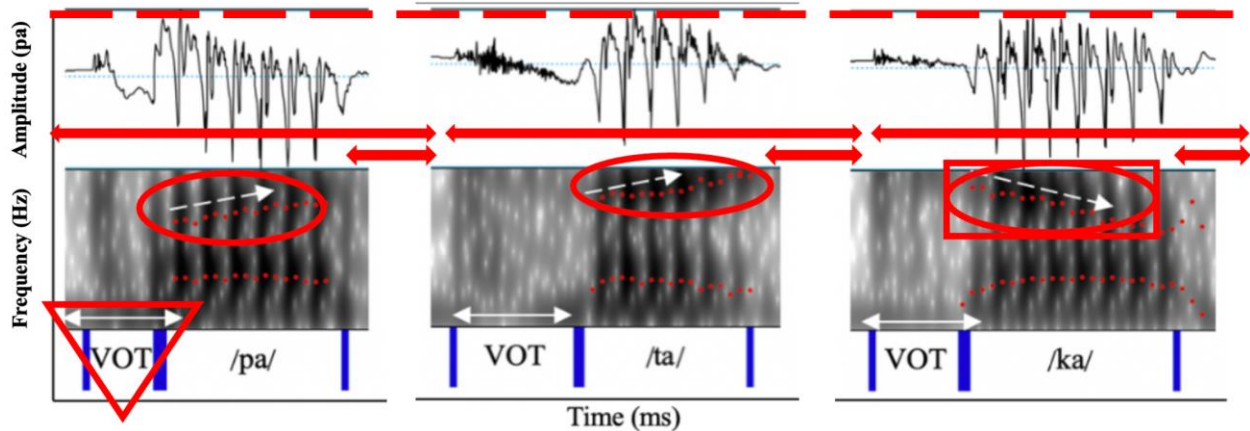


Figure 2. Acoustic spectrogram and waveform of an utterance of /pataka/ produced by a speaker with amyotrophic lateral sclerosis (ALS). Each shape outlines the portions of the signal from which the five components were extracted. 1. Red Arrows = Coordination (proportion of stop gap [i.e., short red arrow] to total syllable length [i.e., long red arrow]); 2. Red Triangle = Consistency (standard deviation of voice onset times [VOT] for each consonant across three repetitions); 3. Red Circles = Precision (standard deviation of three formant slopes for /pa/, /ta/, and /ka/ within each repetition); 4. Red Square = Speed (mean of formant slope for /ka/ across three repetitions); and 5. Red Dashed Line = Rate (syllables produced per second).

Table 3. Description of the components and features for the articulatory phenotypes.

	Definition	Feature	Parsing and Calculation Methods
Coordination	appropriate temporal alignment of movements to meet task demands	<i>Proportion of Stop Gap to Total Syllable Length</i>	<ol style="list-style-type: none"> 1. Parse each syllable from consonant release (defined by amplitude burst on spectrogram) to subsequent vowel offset (defined by final glottal pulse on spectrogram) and from subsequent vowel offset to subsequent consonant release 2. Calculate duration between vowel offset in /pa/ and release of /t/, between vowel offset in /ta/ and release of /k/, and between vowel offset in /ka/ and release of subsequent /p/ (i.e., gaps during syllable transitions) 3. Calculate duration between release of /p/ to release of /t/, between release of /t/ to release of /k/, and between release of /k/ and release of subsequent /p/ (i.e., full syllable length) 4. Calculate average gap duration and average full syllable length 5. Calculate proportion of average gap duration to average full syllable length <p>↑ values = greater gap time during syllable transition and thus ↓ Coordination</p>
Consistency	stability of speech sounds across multiple repetitions	<i>Across-Repetition Variability in Voice Onset Time</i>	<ol style="list-style-type: none"> 1. Parse each consonant from release to subsequent vowel onset (defined by first glottal pulse on spectrogram) 2. Calculate duration between consonant release and subsequent vowel onset for each repetition (i.e., voice onset time [VOT]) 3. Calculate standard deviation in voice onset time between three repetitions and multiply by 100 to obtain coefficient of variation 4. Calculate average standard deviation of VOT across /p/, /t/, and /k/ <p>↑ values = greater variability in voice onset time and thus ↓ Consistency</p>

Speed	quickness of movement during each syllable repetition	<i>Second Formant Slope of /k/ (Hz/ms)</i>	<ol style="list-style-type: none"> 1. Parse each repetition of /ka/ from vowel onset to vowel offset 2. Run custom Praat script to extract formant time series 3. Divide difference between frequency at vowel midpoint and frequency at vowel onset (i.e., F2-F1) by difference between time at vowel midpoint and time at vowel onset (i.e., T2-T1) for consonant-vowel transition in /ka/ (i.e., F2 slope) 4. Calculate average F2 slope across all three repetitions of /pataka/ ↓ values = reduced rate of vocal tract configuration and thus ↓ <i>Speed</i>
Precision	clearness and distinctiveness of consonants	<i>Across-Consonant Variability in Second Formant Slope</i>	<ol style="list-style-type: none"> 1. Parse each repetition of /pa/, /ta/, and /ka/ from vowel onset to vowel offset 2. Run custom Praat script to extract formant time series 3. Divide F2-F1 by T2-T1 for each consonant-vowel transition in /pa/, /ta/, and /ka/ 4. Calculate standard deviation of F2 slope between consonants within each repetition of /pataka/ 5. Calculate average standard deviation of F2 slope across all three repetitions of /pataka/ ↓ values = reduced variability in place of articulation and thus ↓ <i>Precision</i>
Rate	quickness of completion of syllable sequences	<i>Sequential Motion Rate (syll/sec)</i>	<ol style="list-style-type: none"> 1. Parse first three repetitions from release of first /p/ to vowel offset in third /ka/ 2. Divide duration of three repetitions by nine (i.e., number of syllables produced) ↓ values = reduced syllables produced per second and thus ↓ <i>Rate</i>

Statistical Analysis

All statistical analyses were completed in R (R Core Team, 2014).

Interrater and Intrarater Reliability

Interrater and intrarater reliability for the acoustic and perceptual analyses were calculated using ICC (2,1) intraclass correlation coefficient (ICC) (2,1) (i.e., two-way random single measures used for consistency/absolute agreement).

Controlling for Articulatory Severity across Clinical Groups

Between-group differences in articulatory severity (both continuous and categorical) were assessed using a one-way analysis of variance (ANOVA) with Tukey's multiple comparison tests to determine which groups were different from one another.

Controlling for Effect of Remote Data Collection on Formant Slope and Voice Onset Time

For the two groups of speakers that included both remote and in-person data (i.e., ALS and controls), we conducted independent t-tests on severity-matched groups to determine the effect of remote data collection on the second formant slope and voice onset time. If remotely collecting data resulted in systematic noise in the signal, we would expect there to be significant differences between the two groups.

Controlling for Effect of Sex and Age on Speech Performance

Because there were unequal ratios of males and females and different age ranges in each group of speakers, we conducted independent t-tests to examine the effect of sex on each of the five acoustic features and Pearson correlations to examine the relationship of age with each of the five acoustic features.

Presence of Articulatory Phenotypes (Research Question 1)

What are the articulatory phenotypes of neurodegenerative diseases known to have divergent speech motor deficits? (Research Question 1a): To examine whether the overall articulatory profiles of the four clinical groups were different from one another and from controls, we conducted a multivariate analysis of variance (MANOVA) with diagnosis as the independent variable and the five articulatory components as the dependent variables. Post hoc one-way ANOVAs with Tukey’s multiple comparison tests were then conducted to determine which articulatory components were significantly different between groups.

Do the acoustic features measure distinct constructs and, therefore, provide unique information about articulatory function for each neurodegenerative disease? (Research Question 1b): To assess whether the features measured distinct constructs for each neurodegenerative disease, we conducted correlations for each pair of acoustic features. We conducted weighted Pearson correlations for the clinical groups as a whole (due to the unequal sample sizes across groups) and unweighted Pearson correlations for each clinical group individually.

Classification Accuracy of Articulatory Phenotypes (Research Question 2)

What is the efficacy of articulatory phenotypes for classifying divergent neurodegenerative diseases? (Research Question 2a): To examine the classification accuracy of articulatory phenotyping, we used a multivariate linear discriminant analysis (LDA). The goal of this analysis was to identify distinguishing characteristics (i.e., phenotypes) of groups through independent variable weightings, known as discriminant vectors, which optimize the ratio of between-group to within-group variance. Because classical LDA identifies discriminant vectors between two groups, the groups were partitioned for the analysis into binary comparisons (e.g., ALS compared to the other three clinical groups). The predictive performance of the LDA was evaluated using k-fold (k = 5) cross-validation. Importantly, all speakers from the clinical groups in this study were symptomatic and already diagnosed with a neurodegenerative disease. Thus, controls were not included in the LDA because this analysis sought to assess whether speech phenotyping informs differential diagnosis (i.e., confirming which disease each speaker had) rather than disease detection.

Is a profile of articulatory features more diagnostically useful than individual features for neurodegenerative diseases? (Research Question 2b): To compare how the individual features performed compared to the profile of features in classifying the four clinical groups, we conducted *univariate* LDAs with each feature individually. We assessed the accuracy of the LDAs using receiver operating characteristic (ROC) curves. Area under the curve (AUC), sensitivity, and specificity were calculated for each curve. Independent samples t-tests were then used to examine whether there was a statistical difference between the AUCs from the univariate LDAs in Research Question 2b and the multivariate LDA using all five features in Research Question 2a.

RESULTS

Interrater and Intrarater Reliability

ICC (2,1) demonstrated good to excellent interrater reliability for all five components measured acoustically and for the SMR severity ratings (see Table 4).

Table 4. Inter- and intrarater reliability with significance levels (* $p < .05$, ** $p < .01$, *** $p < .001$) for acoustic measures of each component and perceptual ratings of articulatory severity.

Measure	Interrater Reliability	Intrarater Reliability
<i>Coordination (GapSyllProp)</i>	ICC (2,1) = .91 [.79, .96]***	ICC (2,1) = .78 [.51, .91]***
<i>Consistency (RepVar.VOT)</i>	ICC (2,1) = .81 [.69, .88]***	ICC (2,1) = .77 [.63, .86]***
<i>Speed (F2Slope)</i>	ICC (2,1) = .77 [.49, .91]***	ICC (2,1) = .85 [.65, .94]***
<i>Precision (ConVar.F2Slope)</i>	ICC (2,1) = .83 [.53, .95]***	ICC (2,1) = .80 [.52, .93]***
<i>Rate (RepRate)</i>	ICC (2,1) = .99 [.99, 1.00]***	ICC (2,1) = .99 [.99, 1.00]***
Severity		
Articulatory Severity Rating (Continuous)	ICC (2,1) = .74 [.67, .79]***	ICC (2,1) = .86 [.67, .94]***
Articulatory Severity Rating (Categorical)	ICC (2,1) = .67 [.59, .74]***	ICC (2,1) = .76 [.49, .90]***

Controlling for Articulatory Severity across Clinical Groups

A one-way ANOVA revealed a significant effect of categorical severity ratings ($F(3, 174) = 4.72, p < .01$) and continuous severity ratings ($F(3, 174) = 6.44, p < .001$) based on diagnosis. Tukey's multiple comparison tests demonstrated significant differences in categorical severity ratings between speakers with PD and ALS and in continuous severity ratings between speakers with PD and each of the other three clinical groups. Our findings for speakers with PD should thus be considered with the knowledge that this clinical group was significantly less severe than the other three clinical groups. There were no significant differences in severity for any of the other pairs.

Controlling for Effect of Remote Data Collection on Formant Slope and Voice Onset Time

Independent samples t-tests revealed no significant effect of remote data collection on the second formant slope (ALS: $p = .13$; controls: $p = .23$) nor on voice onset time (ALS: $p = .78$; controls: $p = .92$).

Controlling for Effect of Sex and Age on Speech Performance

Independent samples t-tests revealed no significant effect of sex on any of the five acoustic features for each of the five speaker groups, and Pearson correlations revealed no significant associations between age and any of the five acoustic features for each of the five speaker groups.

Presence of Articulatory Phenotypes

What are the articulatory phenotypes of neurodegenerative diseases known to have divergent speech motor deficits? (Research Question 1a): A MANOVA was conducted to determine whether the overall articulatory profiles of the four clinical groups were different from one another and from controls. The multivariate result was significant for all articulatory components (Coordination: $F(4, 212) = 25.04, p < .001$; Consistency: $F(4, 212) = 11.84$; Speed: $F(4, 212) = 8.22$; Precision: $F(4, 212) = 7.87$; Rate: $F(4, 212) = 36.70$), indicating a difference in articulatory performance depending on speaker diagnosis. One-way ANOVAs with Tukey's multiple comparison tests were also conducted to determine which groups were significantly different from one another (see Table 5). Figures 3 and 4 illustrate the articulatory performance of the four clinical groups and controls in raw scores and z scores, respectively.

Do the acoustic features measure distinct constructs and, therefore, provide unique information about articulatory function for each neurodegenerative disease? (Research Question 1b): Weighted and unweighted Pearson correlations were used to assess whether the features measured distinct constructs for each neurodegenerative disease. Our findings revealed weak to moderate correlations for all pairs of acoustic features in the clinical groups as a whole and in each clinical group individually (see Table 6).

Table 5. Effect sizes and confidence intervals for between-group comparisons of performance on the articulatory components. The arrow indicates the group that was more impaired on the component (e.g., when comparing ALS and PA on Consistency, the arrow is pointing left because speakers with PA have more impaired Consistency than speakers with ALS) (* = $p < .05$, ** = $p < .01$, *** = $p < .001$). Statistically significant differences are in bold.

	Control	ALS	PA	PD	nfPPA+PAOS
COORDINATION	Control				
	ALS	↑.48 [.04, .92]			
	PA	↑.25 [-.17, .66]	←.29 [-.11, .69]		
	PD	←.13 [-.27, .53]	←.64* [.23, 1.04]	←.40 [.02, .78]	
	nfPPA+PAOS	←1.80*** [1.12, 2.46]	←1.95*** [1.28, 2.61]	←2.09*** [1.43, 2.74]	←1.93*** [1.31, 2.54]
CONSISTENCY	Control				
	ALS	←.32 [-.11, .75]			
	PA	←.87*** [.41, 1.33]	←.68** [.26, 1.10]		
	PD	↑.35 [-.06, .76]	↑.65 [.24, 1.06]	↑1.14*** [.71, 1.57]	
	nfPPA+PAOS	←.26 [-.28, .80]	←.02 [-.51, .54]	↑.55* [.02, 1.07]	←.54 [.02, 1.05]
SPEED	Control				
	ALS	←.95*** [.47, 1.43]			
	PA	←.73*** [.28, 1.17]	↑.14 [-.26, .54]		
	PD	←.86*** [.41, 1.31]	↑.13 [-.25, .52]	←.03 [-.34, .40]	
	nfPPA+PAOS	←1.29*** [.67, 1.89]	←.42 [-.11, .95]	←.49 [-.04, 1.01]	←.57 [.05, 1.08]
PRECISION	Control				
	ALS	←.96*** [.48, 1.44]			
	PA	←.70** [.25, 1.14]	↑.21 [-.19, .61]		
	PD	←.45 [.03, .86]	↑.49 [.09, .88]	↑.26 [-.12, .63]	
	nfPPA+PAOS	←1.55*** [.91, 2.19]	←.41 [-.13, .94]	←.60 [.07, 1.13]	←.93** [.39, 1.46]
RATE	Control				
	ALS	←1.15*** [.64, 1.64]			
	PA	←1.61*** [1.05, 2.15]	←.18 [-.22, .57]		
	PD	←.78* [.33, 1.21]	↑.60* [.19, 1.00]	↑.93*** [.52, 1.34]	
	nfPPA+PAOS	←3.57*** [2.60, 4.53]	←1.50*** [.89, 2.10]	←1.67*** [1.06, 2.28]	←2.90*** [2.17, 3.62]

Note. ALS = amyotrophic lateral sclerosis; PA = progressive ataxia; PD = Parkinson's disease; nfPPA+PAOS = the nonfluent variant of primary progressive aphasia and progressive apraxia of speech.

Table 6. Correlation matrices of performance on the acoustic features for the clinical groups as a whole and for each clinical group individually (* = $p < .05$, ** = $p < .01$, *** = $p < .001$).

Pairwise Correlations	All	ALS	PA	PD	nfPPA+PAOS
Coordination x Consistency	-.03	.05	-.24	-.15	.68
Coordination x Speed	-.15*	-.07	-.20	-.09	-.30
Coordination x Precision	-.16*	-.13	-.19	-.14	.36
Coordination x Rate	.09	-.08	-.21	.09	.57**
Consistency x Speed	.01	.04	.03	.08	-.08
Consistency x Precision	-.002	.003	-.18	.19	.08
Consistency x Rate	.25***	.10	.22	.09	.33
Speed x Precision	.68***	.73***	.63***	.54***	.17
Speed x Rate	.43***	.58***	.51***	.29*	-.18
Precision x Rate	.58***	.72***	.70***	.31**	.53*

Note. ALS = amyotrophic lateral sclerosis; PA = progressive ataxia; PD = Parkinson’s disease; nfPPA+PAOS = the nonfluent variant of primary progressive aphasia and progressive apraxia of speech.

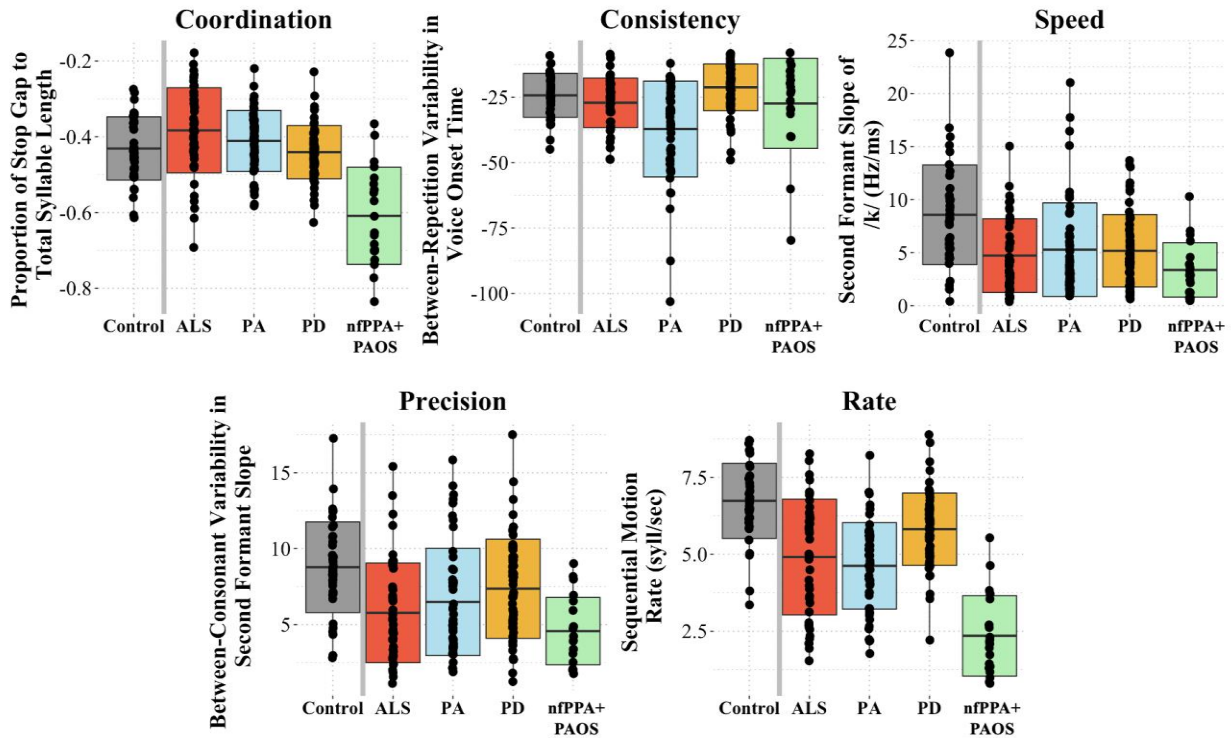


Figure 3. Boxplots demonstrating mean performance on each component of articulatory motor control for the four clinical groups and controls.

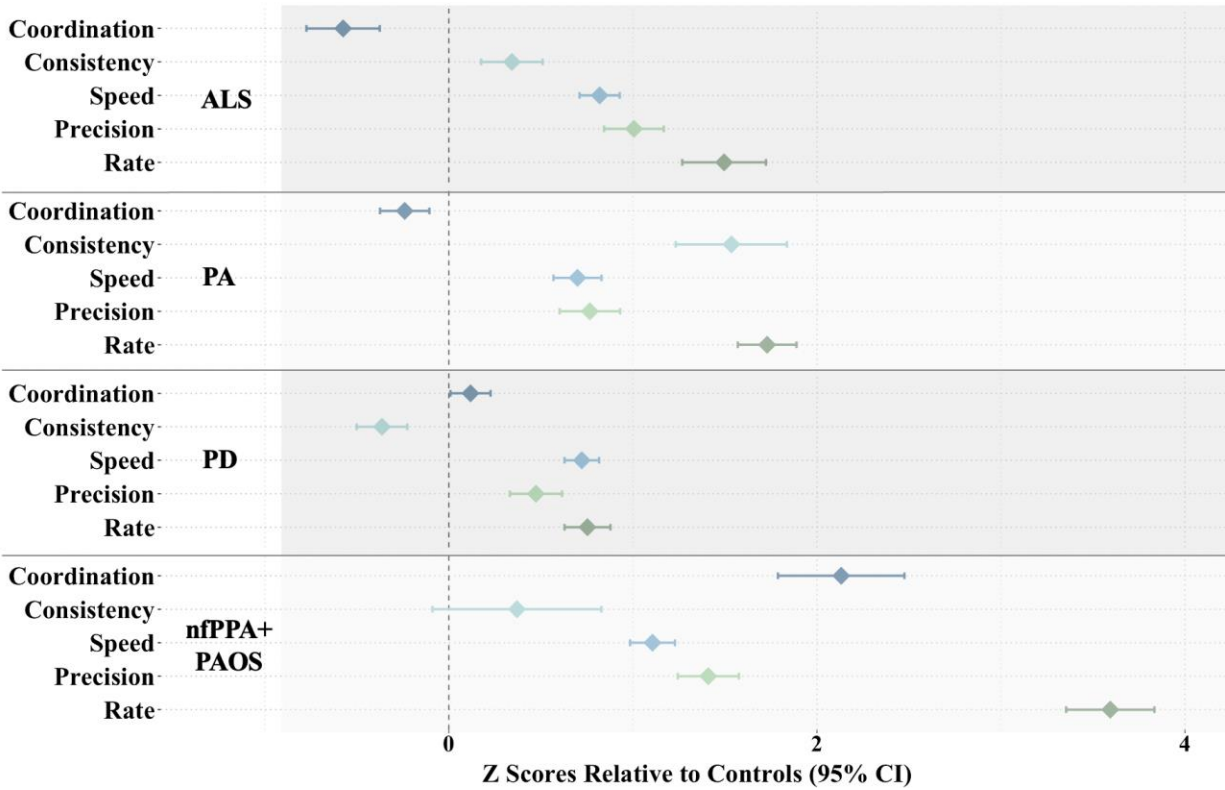


Figure 4. Forest plot demonstrating divergent patterns of articulatory performance across the four clinical groups. Each diamond represents the mean z score (clinical group compared to controls) with the 95% confidence interval (CI) for each articulatory component. Z scores to the right of the vertical dotted line (i.e., positive z scores) indicate that the clinical group is more impaired than controls.

Classification Accuracy of Articulatory Phenotypes

What is the efficacy of articulatory phenotypes for classifying divergent neurodegenerative diseases? (Research Question 2a): Multivariate LDAs with five-fold cross validation were used to determine the classification accuracy of the articulatory profiles for the four clinical groups. ROC curve analyses revealed acceptable to good average AUC, sensitivity, and specificity values for each clinical group except ALS (see Figure 5). Interpretation of ROC performance was based on guidelines described in Safari and colleagues (Safari et al., 2016).

Is a profile of articulatory features more diagnostically useful than individual features for neurodegenerative diseases? (Research Question 2b): Univariate LDAs with five-fold cross validation were also conducted with each of the five features. Independent samples t-tests demonstrated that the average AUC of the clinical groups using the multivariate LDA was significantly higher than the average AUCs of all clinical groups using the univariate LDAs. This finding indicates that the profile of features performed significantly better than individual features at classifying the four clinical groups (see Table 7).

Table 7. Average AUC (in bold), sensitivity, and specificity based on the five cross-validation folds of the univariate (i.e., only including individual features) and multivariate (i.e., including all features) LDAs for the clinical groups as a whole and for each group individually.

	ALS	PA	PD	nfPPA+PAOS	Average AUC for All Clinical Groups	Comparison of Average AUCs for All Clinical Groups
Coord	.69 , .62, .79	.57 , .67, .58	.70 , .74, .69	.88 , .88, .85	.71	Coord-All Features $p < .05^*$
Con	.55 , .66, .55	.75 , .76, .74	.74 , .79, .66	.39 , .53, .52	.61	Con-All Features $p < .001^{***}$
Speed	.36 , .41, .51	.53 , .66, .50	.54 , .60, .63	.63 , .80, .58	.52	Speed-All Features $p < .001^{***}$
Prec	.56 , .73, .51	.43 , .39, .67	.63 , .67, .64	.69 , .73, .69	.58	Prec-All Features $p < .001^{***}$

Rate	.45, .54, .54	.67, .69, .66	.74, .79, .66	.91, .93, .85	.69	Rate-All Features	$p < .05^*$
All Features	.64, .64, .66	.80, .75, .82	.83, .82, .78	.95, .88, .96	.81		

Note. ALS = amyotrophic lateral sclerosis; PA = progressive ataxia; PD = Parkinson’s disease; nfPPA+PAOS = the nonfluent variant of primary progressive aphasia and progressive apraxia of speech.

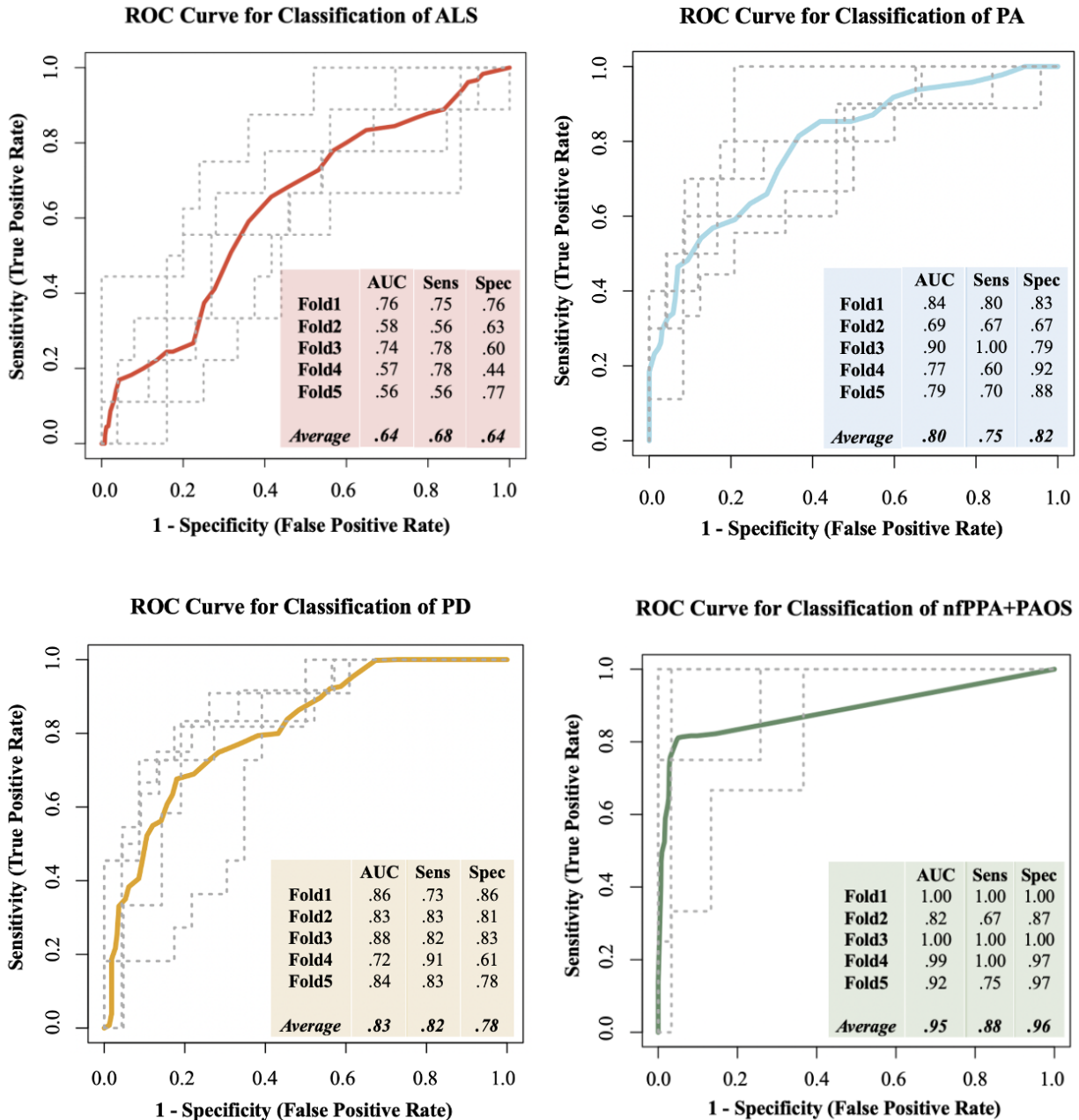


Figure 5. Receiver operating characteristic (ROC) curves based on the linear discriminant analysis (LDA) for each clinical group. Area under the curve (AUC), sensitivity, and specificity values are given for each of the five validation folds, along with the averages of each.

DISCUSSION

Overall, there were three central findings of our study: (1) The clinical groups exhibited unique articulatory phenotypes, with the primary distinguishing features of reduced Consistency for speakers with PA, preserved repetition Rate for speakers with PD, and reduced Coordination and repetition Rate

for speakers with nfPPA+PAOS; (2) The articulatory features provided unique information about speech motor performance for each clinical group, as indicated by weak to moderate pairwise comparisons for most pairs of acoustic features; and (3) Classification accuracy was better for acoustic-based profiles than for individual features, with acceptable to good sensitivity *and* specificity for all clinical groups except speakers with ALS.

Presence of Articulatory Phenotypes

PD Phenotype: Impaired Speed and Rate Compared to Controls, but Preserved Rate Compared to Other Clinical Groups

For speakers with PD, the finding of decreased Speed relative to controls is consistent with the DAB classification of hypokinetic dysarthria, which posits that hypokinesia leads to reduced movement size and speed (Darley et al., 1969a, 1969b). Moreover, acoustic studies have demonstrated reduced second formant slope in speakers with PD (Chiu et al., 2019; Connor et al., 1989; Kim et al., 2009; Martel-Sauvageau & Tjaden, 2017; Rosen et al., 2006; Tjaden et al., 2013; Tjaden & Wilding, 2004; Walsh & Smith, 2012; Weismer et al., 2001). Our finding of preserved repetition Rate relative to the other clinical groups also aligns with previous acoustic work examining multiple clinical groups, which demonstrated less impaired repetition Rate in speakers with PD compared to those with ALS (Rowe et al., 2020), PA (Ziegler, 2002), MS (Tjaden & Watling, 2003), and MSA-C (Rusz et al., 2019). Similarly, Darley and colleagues identified short rushes of speech or increased rate as a hallmark characteristic of basal ganglia damage (Darley et al., 1969a, 1969b). Researchers have thus proposed that Speed and Rate can dissociate in speakers with PD (Weismer & Berry, 2003). These acoustic findings align with expectations advanced in the literature on the neural mechanisms of hypokinetic dysarthria due to PD (Braak et al., 2003; Guenther, 2016). Indeed, a loss of cortical regulation due to damage to the basal ganglia (Braak et al., 2003) may result in slowed movement Speed. Simultaneously, impaired signaling of when to execute the subsequent speech motor unit may reduce the duration of motor programs, resulting in "bursts of rapid speech" or increased Rate (Guenther, 2016). The neurological abnormalities underlying impaired Rate, in particular, may be more widespread, as recent work found that Rate remained unchanged for speakers with basal ganglia deficits (Rusz, Tykalova, Novotny, Zogala, et al., 2021).

Contrary to prior work, Precision was not significantly reduced compared to controls or the other clinical groups. This finding was surprising given that hypokinesia secondary to PD has been known to downscale articulatory displacements (Ackermann & Ziegler, 1991; Darley et al., 1969a, 1969b; Darling & Huber, 2011; Forrest et al., 1989; Walsh & Smith, 2012; Yunusova et al., 2008, 2011). Numerous studies have found that speakers with PD tend to have reduced vowel dispersion compared to speakers with ALS (Mefferd, 2015), reduced vowel area index compared to speakers with PSP (Skodda et al., 2012), reduced consonant closure compared to speakers with HD and PA (Ackermann et al., 1995), and reduced second formant interquartile range compared to speakers with MS (Kuo & Tjaden, 2016). Given these prior findings, it is possible that second formant slope variability does not adequately capture the imprecision characteristic of hypokinetic dysarthria. However, our negative findings for Precision may also be due to the mild severity of the speakers. Additional work is needed to further investigate the manifestation of imprecision in speakers with PD across the severity continuum.

In sum, the articulatory phenotype of PD in our study tended to be less impaired than those of the other speakers, but two notable articulatory abnormalities were (1) reduced Speed and repetition Rate relative to controls and (2) preserved repetition Rate relative to speakers in the other clinical groups.

nfPPA+PAOS Phenotype: Impaired Coordination, Speed, Precision, and Rate Compared to Controls, but Only Impaired Coordination and Rate Compared to Other Clinical Groups

For speakers with nfPPA+PAOS, our findings align with the primary perceptual speech characteristics associated with PAOS: slow rate, distorted substitutions, syllable segregation, excess/equal stress, and poorly sequenced SMRs (Duffy, 2006; Duffy et al., 2021). First, our finding of impaired Speed and Rate align with the perceptual characteristic of slow rate, which is also consistent with recent acoustic work demonstrating reduced articulatory and repetition Rate and lengthened vowels in PAOS (Cordella et

al., 2017, 2019; Duffy et al., 2015, 2017; Laganaro et al., 2012; Takakura et al., 2019; Utianski et al., 2018; van der Merwe, 2009; Wilson et al., 2010). Similarly, our finding of reduced Coordination may capture perceptual characteristics of PAOS such as syllable segregation and poorly sequenced SMRs. Indeed, we found that speakers with nfPPA+PAOS produced abnormally long gaps before each new syllable (i.e., between /pa/ and /ta/, /ta/ and /ka/, and /ka/ and subsequent /pa/). Prior work has demonstrated similar findings of segmented syllables both in speakers with PAOS (Bouvier et al., 2021; Duffy, 2006; Takakura et al., 2019) and non-degenerative AOS (Deger & Ziegler, 2002; Kent & Rosenbek, 1983; Melle & Gallego, 2012; Staiger & Ziegler, 2008). While pausing between syllables could be a compensatory behavior, pausing during a maximum performance task, in which speakers are asked to repeat sounds as quickly as possible, is more likely indicative of the extra time needed to sequence and specify the motor program (Strand et al., 2014). Atypical pausing between syllables may also be associated with articulatory groping (Shriberg et al., 2017a, 2017b, 2017c, 2017d). Neural models of AOS have proposed that groping reflects an inability to access subsequent speech units from the left premotor cortex (Guenther, 2016; Miller & Guenther, 2021). From this perspective, the observed longer gaps in the nfPPA+PAOS group can be interpreted as discoordination at the planning level. Research continues to explore the link between areas of brain atrophy (e.g., gray matter of premotor, supplementary motor, and primary motor cortices, bilaterally; Josephs et al., 2012) and the clinical manifestations of PAOS.

One surprising finding for this clinical group was preserved Consistency using across-repetition variability in VOT. This finding was surprising considering prior work which has shown that changes in VOT are sensitive to incorrect sound productions in speakers with AOS (Wambaugh et al., 1997), and sound substitutions are a common error type in AOS (Strand et al., 2014). However, although VOT tends to change as position of occlusion changes (Baum & Ryan, 1993; Klatt, 1975), the range of VOT values can overlap across different voiceless sounds (Auzou et al., 2000). Therefore, inconsistencies in substitution patterns may not have been evident using our Consistency measure with this specific task.

In sum, the articulatory phenotype of nfPPA+PAOS in our study was characterized by (1) impaired Coordination, Speed, and repetition Rate relative to controls and (2) impaired Coordination and repetition Rate relative to speakers in the other clinical groups.

PA Phenotype: Impaired Consistency, Speed, Precision, and Rate Compared to Controls, but Only Impaired Consistency Compared to Other Clinical Groups

Consistent with our findings, deficits in Speed, Precision, and Rate have been documented in prior acoustic work on speakers with PA (*Speed*: Folker et al., 2012; Lansford & Liss, 2014; *Precision*: Folker et al., 2012; Skodda et al., 2013; *Rate*: Ozawa et al., 2001; Schalling et al., 2007; Singh et al., 2010; Tykalova et al., 2016) and in the DAB classification of ataxic dysarthria (Darley et al., 1969a, 1969b). Our finding of reduced Consistency in speakers with PA relative to controls is also congruent with prior work (Brendel et al., 2015; Darley et al., 1969a, 1969b; Gentil, 1990; Kashyap et al., 2018; Portnoy & Aronson, 1982; Tykalova et al., 2016), which reflects the effects of cerebellar damage on motor function in individuals with PA (Schmahmann, 2004). Indeed, the cerebellum is thought to regulate the timing among movements in a sequence (Guenther, 2016; Spencer & Slocumb, 2007; Tourville & Guenther, 2011), particularly for behaviors that involve explicit temporal goals (Ivry et al., 2002; Schmitz-Hübsch et al., 2012), such as the SMR task. Thus, in contrast to the substitution errors seen in speakers with nfPPA+PAOS, inconsistency secondary to cerebellar deficits can manifest as variability in movement timing (Ziegler et al., 1993; Ziegler & Wessel, 1996), such as timing of laryngeal control, which was reflected in our measure of across-repetition variability in VOT. Beyond appropriate timing of movements, the cerebellum is responsible for fine-tuning or refining movements (Chiu et al., 1996; Guenther, 2016; Kent et al., 1979). Several authors have hypothesized that in ataxic dysarthria, feedforward motor commands are disrupted, which forces the motor control system to rely on sensory feedback commands (Guenther, 2016; Parrell et al., 2017). The reliance on sensory feedback, which requires longer delays, may result in lengthened speech segments (Kent et al., 1979) and, therefore, may contribute to findings of reduced Speed and Rate in speakers with PA.

Our finding of intact Coordination was surprising given that incoordination is often cited as a key deficit associated with cerebellar dysfunction (Ackermann et al., 2007; Ackermann & Hertrich, 1997; Darley et al., 1969a, 1969b; Kent et al., 1979, 1997; Tykalova et al., 2016; Vogel et al., 2018). Furthermore, previous work has identified increased gap durations for speakers with ataxia in the DDK task (Ozawa et al., 2001; Schalling et al., 2007; Schalling & Hartelius, 2004). However, we examined the *proportion* of gap to syllable duration, which will be smaller if the syllable is longer. Ozawa and colleagues also examined this proportion in speakers with ataxia and, similar to our results, found no significant differences from controls (Ozawa et al., 2001). The results for speakers with PA in conjunction with those of the nfPPA+PAOS group suggest that incoordination may manifest differently depending on the neurological/pathophysiological abnormalities. Indeed, while both AOS and ataxic dysarthria may lead to disruptions in motor planning/programming (Kent et al., 1997, 2000; Spencer & Rogers, 2005), cortical thinning in the left frontal lobe—as seen in AOS—may manifest in difficulty with accessing the motor plan for the subsequent gesture, which we quantified using a measure of syllable transition; on the other hand, cerebellar deficits—as seen in ataxic dysarthria—may be best quantified using measures of movement smoothness to reflect deficits in timing (Chang et al., 2005; Mark & Steve, 1993). The distinction in how Coordination manifests depending on the loci of neurological deficit highlights the need for more than one operational definition of Coordination. Identifying the precise construct of interest will allow researchers to develop quantitative measures that more accurately represent the articulatory deficit specific to a certain clinical group. Importantly, prior work has shown that speakers with ataxic dysarthria tend to perform better on SMRs than on AMRs (Duffy, 2013), which may have also contributed to our null findings for Coordination. In addition to the influence of task, our findings may have been influenced by our assessment of only three repetitions, as it is possible that such a small number of repetitions is insufficient for capturing discoordination in this population. Future work should further investigate measures of Coordination—in a more sensitive task for the population (i.e., AMRs, more repetitions)—that can detect the coordinative deficits characteristic of speakers with PA.

Taken together, the articulatory phenotype for speakers with PA in our study was characterized by (1) deficits across all articulatory components except Coordination (as indexed by intersyllabic pausing) relative to controls and (2) impaired Consistency relative to the other clinical groups.

ALS Phenotype: Impaired Speed, Precision, and Rate Compared to Controls, but No Salient Differentiator from Other Clinical Groups

In contrast to hypokinetic dysarthria, AOS, and ataxic dysarthria, the neural mechanisms underlying mixed spastic-flaccid dysarthria secondary to ALS are less conclusive. Flaccid dysarthria results from damage to the lower motor neurons (LMNs), which are known as the final common pathway for transmitting neural information to the muscles. The nerves that are involved thus determine which articulators are affected. For example, an impaired trigeminal nerve will likely result in jaw weakness and an impaired hypoglossal nerve will likely result in tongue weakness. Although the disease initially manifests in different body locations depending on the person (e.g., some speakers initially present with tongue weakness, whereas others may present with leg weakness), eventually all nerves become affected, which, in the case of speech, results in broad deficits across multiple articulatory domains (Samlan & Weismer, 1995; Weismer & Green, 2015). Darley and colleagues posit that this general reduction in muscle strength may contribute to imprecise consonant production in speakers with flaccid dysarthria (Darley et al., 1969a, 1969b), which aligns with our findings and those in prior acoustic studies (Lee et al., 2017; Lee & Fischer, 2019; Turner et al., 1995; Yunusova et al., 2005, 2012).

The spastic component of dysarthria involves damage to the upper motor neurons (UMNs), which are responsible for carrying information from the primary cortex to the LMNs. Damage to the UMNs is associated with muscle spasticity, which may result in slow and labored speech (Darley et al., 1969a, 1969b; Langmore & Lehman, 1994). Indeed, consistent with previous acoustic literature, we found reduced Speed and repetition Rate in speakers with ALS (*Speed*: Lansford & Liss, 2014; Mulligan et al., 1994; Weismer et al., 1992, 2001; Yunusova et al., 2012; *Rate*: Mulligan et al., 1994; Rong, 2020; Shellikeri et al., 2021).

In sum, a divergent profile for ALS emerged when examining differences in the five articulatory components relative to controls. No articulatory components, however, distinguished speakers with ALS from the other three clinical groups. This finding may reflect the heterogeneity in bulbar involvement and neuropathology across individuals with ALS (DePaul et al., 1988; Langmore & Lehman, 1994; Lawyer & Netsky, 1953; Shellikeri et al., 2017; Stipancic et al., 2021). Future work is needed to further investigate the potential within-group phenotypic variability in speakers with ALS.

Lack of Redundancy among Acoustic Features Regardless of Clinical Diagnosis and Different Relationships between Acoustic Features Depending on Clinical Diagnosis

An important consideration in this study was whether the five features were assessing different constructs and, therefore, contributing unique information to the characterization of articulatory function for each neurodegenerative disease. This objective is typically addressed by examining pairwise correlations between the constructs that are hypothesized to be distinct (Streiner & Norman, 2015). Overall, examining the associations between performance on the acoustic measures demonstrated (1) a lack of redundancy among the five acoustic features regardless of the clinical diagnosis and (2) different relationships between features depending on the clinical diagnosis. First, pairwise analyses revealed weak to moderate correlations between most pairs of acoustic features for the clinical groups as a whole and for each clinical group individually, which indicates a lack of redundancy in the measures and that investigating all five constructs may be important for fully characterizing articulatory function for each disease. Although two of the measures (i.e., Coordination and Consistency) have since been updated, the weak to moderate correlations we found in this study are consistent with our prior work assessing the divergent validity of the five features in this framework (Rowe et al., 2021; Rowe & Green, 2019). Importantly, while only a small number of the associations in the individual clinical group results were significant (two to three out of 10 per clinical group), including all participants in the analysis resulted in more significant correlations (five out of 10 for the whole group). This finding suggests that the lack of significant associations in the individual group results may be related to insufficient statistical power.

We also found distinct relationships between articulatory constructs depending on the clinical group, which may provide additional disease-specific knowledge about the manifestation of different neurological deficits. For example, Speed and Precision were strongly correlated in speakers with ALS but exhibited a negligible association in speakers with nfPPA+PAOS. The strong positive correlation in ALS suggested that most speakers who exhibited reduced Speed also exhibited reduced Precision, which may reflect the uniform effects of muscle weakness on these articulatory constructs. While a correlation of .73 does not indicate redundancy or multicollinearity, a strong correlation between these two constructs suggests that, for speakers with ALS, measuring Speed and Precision will provide similar information about articulatory function. The weak Speed-Precision relationship in speakers with nfPPA+PAOS, on the other hand, indicate that performance on the two constructs may diverge in this population. Interestingly, the correlation between Speed and displacement, the latter of which is a measure of Precision, has been used in prior studies to index neuromuscular coordination, with lower correlations indicating a decoupling of motor systems (Missitzi et al., 2004). Thus, the differences in the Speed-Precision relationship in ALS compared to nfPPA+PAOS offer further information about articulatory function for each group.

Classification Accuracy of Articulatory Phenotypes

Use of Individual Features versus Profiles of Features for Classifying Clinical Groups

In addition to validating the use of our acoustic-based framework for *characterizing* articulatory abnormalities across multiple divergent populations, this study investigated its utility for *classifying* neurodegenerative diseases. To that end, it was important to consider whether a profile of features was more diagnostically useful than individual features. When considering all five acoustic measures in the classification of the four clinical groups, our ROC analysis based on the multivariate LDA yielded good to excellent average AUCs for distinguishing PA (.80), PD (.83), and nfPPA+PAOS (.95) from the other clinical groups but a poor average AUC for distinguishing ALS (.64). One potential reason for the poor

performance in classifying ALS is the lack of significant differences in articulatory performance in the between-clinical group comparisons, which may be related to the subtypes within ALS, such as bulbar-versus spinal-onset or spastic- versus flaccid-dominant dysarthria.

Consistent with prior work (Ballard et al., 2016; Basilakos et al., 2017), we found that a combination of features exhibited stronger performance than individual features with classifying clinical groups, suggesting that a profile was able to capture the diversity in articulatory abnormalities more adequately across groups. Both Ballard and Basilakos and colleagues (2016 and 2017, respectively) demonstrated that combining measures that were significantly impaired in AOS (e.g., pairwise variability index and envelope modulation spectrum) resulted in improved classification accuracy (Ballard et al., 2016; Basilakos et al., 2017). The improvement in performance in our study, however, may provide support for examining features that are both impaired *and* spared. Indeed, a closer examination of the univariate analysis revealed that even features that were unaffected, such as Coordination in ALS and Consistency in PD, exhibited acceptable specificity and/or sensitivity for classification of the respective clinical groups. Taken together, our findings suggest that the acoustic-based profiles we identified in this study have promising clinical utility for informing the classification of PA, PD, and nfPPA+PAOS.

LIMITATIONS

There are several limitations of this study. While we assigned acoustic features to each articulatory component based on descriptions and definitions used in prior literature, the components can manifest in a variety of ways. Our definition of "appropriate temporal alignment of movements to meet task demands" can subsume coordinative indices such as movement smoothness, motor equivalence, and timing/sequencing (Caruso et al., 1988), all of which can be measured using different features. Thus, a measure that reflects Coordination for one population may not detect this deficit in another population known to have incoordination, as we saw in our findings for speakers with PA.

Second, although our statistical testing suggested that remotely recording speech using the Beive app had no measurable effect on the acoustic features we extracted, more work is needed to understand the potential limitations of using smartphone-based speech analytic platforms for recording speech in a home setting.

Third, while we controlled for articulatory severity in the ALS, PA, and nfPPA+PAOS groups by restricting the severity range, there were significant differences in categorical severity ratings between PD and ALS, and in continuous severity ratings between PD and all other clinical groups. Although the severity ratings of all four clinical groups were similar, additional work is needed to examine the articulatory phenotypes of groups that are fully matched on articulatory severity. Similarly, we controlled for sex and age by conducting independent t-tests and Pearson correlations, respectively, which revealed no significant differences or correlations with the acoustic measures. However, it is important to note that lack of significant effects does not indicate that there was no influence of these variables on our findings. Indeed, two recent studies demonstrated a significant effect of sex and age on voice onset time and sequential motion rate in de-novo Parkinsonian speakers with and healthy controls (Rusz et al., 2022; Rusz, Tykalova, Novotny, Ruzicka, et al., 2021). Thus, our findings should be considered within the context of this work.

Furthermore, our study did not consider potential subtypes within each clinical group (e.g., bulbar- versus spinal-onset ALS, phonetic versus prosodic PAOS, tremor-dominant PD versus PD characterized by postural instability and gait disorders). Similarly, speakers in the nfPPA+PAOS group may perform differently on the SMR task depending on their level of concomitant aphasia (Henry et al., 2016), as speakers with severe aphasia may produce more errors that are driven by phonological deficits rather than motoric deficits. While PPA and PAOS often co-occur in neurodegenerative cases (Gorno-Tempini et al., 2011), PAOS can exist in the absence of aphasia (Josephs et al., 2012). Future work should, therefore, investigate primary PAOS in speakers with no/negligible aphasia to further contribute to our understanding of the articulatory characteristics in the potential phonetic and prosodic subtypes of primary PAOS (Utianski et al., 2018). Overall, identifying the articulatory characteristics that distinguish

clinical subtypes would provide valuable information that may further inform diagnostic and treatment decision-making.

Given that some of the data were acquired from secondary sources, we did not have access to disease severity, disease duration, and medication status for all participants in the study. While not controlling for these variables may limit the generalizability of our findings, we do not view the absence of this information as a confound for our results. The purpose of this study was to examine disease classification accuracy based solely on speech function, and there are many cases where speech severity is distinct from disease severity, duration, or medication use (Ball et al., 2002; Barnett et al., 2020; Cavallieri et al., 2021; Fabbri et al., 2017; Rusz, Tykalova, Novotny, Zogala, et al., 2021; Skodda, Flasskamp, et al., 2011; Tykalova et al., 2022). Thus, given the study's focus on speech function, we believe the most critical component to control for was speech severity.

Finally, although weak pairwise correlations suggest a lack of redundancy in the five features, we cannot conclude that the five components are all necessary and sufficient for characterizing articulatory function. In addition, while we found that the multivariate LDA performed better than the univariate LDAs in classifying the clinical groups, we did not examine the performance of different combinations of the five features (e.g., Coordination and Rate), and we do not know the extent to which adding even more features will further increase the classification accuracy. As indicated in the Methods, the features we used to represent each component are considered candidate measures that should be used to generate testable hypotheses and continually revisited and refined in light of new knowledge or evidence. Similarly, we derived our features from the SMR task, which may reveal different articulatory deficits than would a connected speech task. A sentence production task, for example, would allow for a more functional assessment of the speaker's articulatory abilities in different phonetic contexts. Future work is thus needed to further investigate the optimal task and number of features for both characterizing and classifying neurodegenerative diseases.

CONCLUSIONS AND CLINICAL IMPLICATIONS

This study sought to assess the articulatory phenotypes of four neurodegenerative populations known to have divergent speech motor deficits and determine the efficacy of articulatory phenotyping for classifying different diseases. We aimed to address a primary limitation of the current differential diagnosis literature by expanding the range of neurological/pathophysiological deficits and articulatory characteristics examined in one study. We found evidence of distinct articulatory phenotypes for the four clinical groups (i.e., ALS, PA, PD, and nfPPA+PAOS), which highlights the phenotypic variability present across neurodegenerative diseases. Additionally, the phenotypes demonstrated strong classification accuracy for characterizing neurodegenerative diseases, which emphasizes the potential clinical utility of using a comprehensive profile of articulation. With further research, speech phenotyping could (1) provide diagnostic information about different movement disorders and (2) guide the development of sensitive outcome measures. Future work should continue to investigate the efficacy of this framework for identifying articulatory profiles across and *within* speech motor populations and for developing new features that best reflect the articulatory characteristics of populations with divergent neurological/pathophysiological deficits.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from MGH, New York University, University of Buffalo, University of Strathclyde, and University of Washington, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the respective institution.

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