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Defining Differences in Patient Characteristics Between Spasmodic Dysphonia and Laryngeal Tremor

Priyesh N Patel, MD¹, Edmond K Kabagambe, DVM MS PhD^{1,2}, Jennifer C Starkweather, MS CCC-SLP¹, Matthew Keller, BS³, Zaki A Ahmed⁴, Simone C Gruber⁴, Jordan S Akins⁴, C. Gaelyn Garrett, MD¹, and David O Francis, MD MS⁵

¹Vanderbilt Voice Center, Department of Otolaryngology, Vanderbilt University Medical Center, Nashville, TN

²Division of Epidemiology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN

³Saint Louis University School of Medicine, St. Louis, MO

⁴Vanderbilt University, Nashville, TN

⁵Division of Otolaryngology, Wisconsin Surgical Outcomes Research, Department of Surgery, University of Wisconsin, Madison, WI

Abstract

Objective—To compare presenting characteristics of patients with adductor spasmodic dysphonia (ADSD), ADSD with laryngeal tremor (ADSD + LT), and laryngeal tremor without ADSD (LT)

Design—Cross-sectional analysis

Methods—Patients treated for laryngeal movement disorders (1990–2016) were included. ANOVA and Chi square tests measured differences in patient characteristics across the three disease groups. Using ADSD as the referent, multivariable logistic regression models were used to determine whether potential risk factors including patient demographics, family history, presence of potential inciting events prior to disease onset, and co-prevalent movement disorders were associated with ADSD+LT or LT.

Results—In all, 652 patients with ADSD (n=377), ADSD + LT (n=98), and LT (n=177) were included. ADSD patients were significantly younger than those with ADSD + LT and LT (52.5±13.4, 63.9±11.3, and 69.3±10.5 years, respectively; p<0.001). Co-prevalent movement disorders were more common in ADSD + LT (38.7%) and LT (57.1%) groups than in the ADSD group (11.5%; p<0.001). Compared to ADSD, patients with ADSD + LT and LT were more likely to develop an additional movement disorder during follow-up. In multivariable analyses,

Corresponding Author: David O. Francis, MD MS, Division of Otolaryngology, Department of Surgery, 600 Highland Ave K4/7, Madison, WI 53792-7375, P. 608.262.8693, F. 608.252.0940, dofrancis@wisc.edu.

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increasing age, female gender, and having a movement disorder at presentation were associated with significantly greater odds of having ADSD + LT or LT when compared to ADSD.

Conclusion—ADSD + LT patients demonstrate intermediate gender composition and age distributions between those with ADSD and LT. These findings suggest that ADSD + LT may be a distinct phenotype in the spectrum of laryngeal movement disorders.

INTRODUCTION

Laryngeal movement disorders are rare and heterogeneous and include spasmodic dysphonia and laryngeal tremor. Clinically, they manifest with involuntary movements of the intrinsic laryngeal musculature and have significant quality of life consequences.^{1–4} Spasmodic dysphonia is a focal dystonia that is characterized as either adductor (ADSD), abductor (ABSD), or mixed.^{5–7} ADSD represents 82–92% of all spasmodic dysphonia cases and is the most studied laryngeal dystonia.^{6,8,9}

Tremors of the larynx involve involuntary rhythmic phonatory breaks that can occur in multiple axes: lateral, vertical, anterior-posterior, or mixed. Lateral laryngeal tremors (LT) principally involve the intrinsic laryngeal adductor muscles (thyroarytenoid [TA], lateral cricoarytenoid [LCA] m.), while other types involve extra-laryngeal musculature. In certain cases, differentiating tremor from ADSD can be difficult.^{10,11} A linkage between these conditions is hypothesized since tremor occurs concomitantly in 26–53% of ADSD cases.^{6,7,10–16} This wide range may reflect clinical similarities of these disorders and lack of consensus diagnostic criteria for ADSD with concomitant tremor (ADSD + LT).^{17–20} Tremors occurring with dystonias have irregular amplitudes and variable frequency relative to essential tremor, although both are action tremors.^{17–20} Recent functional imaging data suggests that ADSD+LT and laryngeal tremor may exist on a spectrum.²¹ Regardless of laryngeal movement disorder, the current gold standard treatment is onabotulinumtoxin A (BTX, Allergan, Irvine, CA, U.S.A.) injection into the overactive laryngeal musculature. Most available data suggests that BTX is more efficacious for ADSD than for laryngeal tremor.^{1,22–26}

Laryngeal movement disorders are rare diseases (<1/100,000 persons),²⁷ thereby limiting aggregation of patients to sufficiently power epidemiologic, pathophysiologic, or comparative interventional studies. Available data suggest that spasmodic dysphonia is diagnosed at a younger age (39–56 years^{2,6,8,9,15,28–31}) than laryngeal tremor (62–72 years^{24–26,32}). Reasons for this discrepancy are unclear. Beyond age, it remains uncertain how patient characteristics with ADSD, ADSD + LT, and LT compare.^{6,13–16}

Better understanding how patient characteristics differ among these conditions may provide insight into pathophysiology, diagnosis, and prognostic outcomes with BTX. A previous series from our center (n=168) has commented on patient characteristics of SD but not tremor patients.³⁰ As our center cares for a large cohort of patients with these rare laryngeal movement disorders, it allows for the study of differentiating characteristics. As such, this study aims to compare presenting patient characteristics between those with 1) ADSD, 2) ADSD + LT, and 3) LT.

MATERIALS AND METHODS

This study was performed in accordance with the Declaration of Helsinki, Good Clinical Practice, and regulatory requirements. Vanderbilt University's Institutional Review Board approved this study (IRB#151020).

Diagnostic Approach

Laryngologists and voice-specialized speech language pathologists collaboratively diagnosed patients with spasmodic dysphonia and laryngeal tremor using standardized phonatory tasks combined with flexible laryngoscopic examination. Stroboscopy videos were reviewed by a speech-language pathologist and a laryngologist to confirm diagnoses recorded in the medical record. Laryngeal tremors were categorized based on directionality (Table 1). Of tremors, the Isolated lateral variant involves analogous adductory laryngeal muscles (TA/LCA m.) as those known to be hyperactive and treated in ADSD. As such, patients with lateral tremor are thought to receive greater benefit from BTX treatment into adductory muscles compared to other tremor directionalities. TA/LCA treatment does not address extralaryngeal sources of tremor responsible for non-lateral tremors.³³ Therefore, patients with lateral tremor directionality are selected for BTX treatment at our center. In this study, laryngeal tremor refers to only those with an isolated lateral directionality that was present during phonation and/or rest.

Patient Population

Patients diagnosed and treated for ADSD, ADSD+LT, and LT between January 1990 and September 2016 were included. Patients with ABSD, mixed spasmodic dysphonia (ADSD +ABSD), and mixed (e.g., lateral and vertical) laryngeal tremors were excluded.

Variables Collected

Medical record data extraction was performed by an investigator and confirmed by a second independent investigator to ensure data quality and accuracy. Patient characteristics collected included age at presentation, gender, race, employment status, self-reported inciting events, family history of tremor or spasmodic dysphonia, and whether they were diagnosed with incident neurologic/movement disorders during follow-up. Smoking and alcohol use were assessed at time of presentation and classified as prior, current, and never used. Co-prevalent neurologic/movement disorders not involving the larynx (e.g., essential tremor of the hand) were diagnosed by neurologists. Anxiety and depression were considered clinically relevant if patients were being actively treated for these at presentation.

Statistical analysis

Data were checked for quality, updated where necessary, and analyzed using Statistical Analysis Software version 9.4 (SAS Institute, Cary, NC). We computed descriptive statistics between patients with ADSD, ADSD+LT, and LT with regard to hypothesized risk factors shown in Table 2. Significance of differences across groups was tested using ANOVA for continuous variables and the chi square test for categorical variables. Using ADSD as a referent, we fitted logistic regression models to determine risk factors for ADSD+LT and LT in which variables hypothesized to contribute to these conditions were entered into the

model simultaneously. In these models, family history of SD and family history of tremor were discarded because of sparse data. In an additional logistic regression with the same potential risk factors as ADSD+LT and LT, we compared LT to ADSD+LT. We estimated odds ratios (OR) and corresponding 95% confidence intervals (CI) for each potential risk factor. To assess robustness of our findings, we also fitted a multinomial logistic regression with generalized logits in which we set ADSD alone as the referent disease category. Differences with $P \leq 0.05$ were considered statistically significant.

RESULTS

Of 817 laryngeal movement disorders patients, 652 met inclusion criteria (ADSD $n=377$, ADSD+LT $n=98$, LT $n=177$). Exclusions are shown in Figure 1. Comparisons of patient characteristics stratified by category are summarized in Table 2. Patients with ADSD were diagnosed at a younger age than those with ADSD+LT or LT: mean 52.5 vs. 63.9 vs. 69.3 years, respectively ($p<0.001$). Females predominated in all groups, but had higher prevalence in the ADSD+LT and LT groups. Race was white in the majority and did not statistically differ between groups. A higher percentage of patients diagnosed with ADSD were employed ($p<0.001$) and presently used tobacco ($p<0.001$) and alcohol ($p=0.04$). In all groups, the majority of patients (75%) did not perceive an inciting event for their movement disorder, and among those who did, the types of inciting events (e.g., upper respiratory infection, psychological trauma, surgery) were similar between groups ($p=0.29$). A family history of tremor was more likely among those with a tremor component than ADSD alone ($p<0.001$).

Co-Prevalent Movement Disorders

At presentation, co-prevalent non-laryngeal movement disorders were most common among patients diagnosed with ADSD+LT or LT (ADSD: 11.5%, ADSD+LT: 38.7%, LT 57.1%, $p<0.001$). Table 3 summarizes the distribution of these movement disorders. Non-laryngeal essential tremor comprised the majority of co-prevalent movement disorders in all groups, but significantly higher percentages were noted in those with ADSD+LT and LT. Patients with ADSD+LT had the highest co-prevalence of non-laryngeal dystonia (i.e., craniocervical or limb dystonias) compared to other groups.

Development of New Movement Disorders

Patients without co-prevalent movement disorders were followed to evaluate whether they developed additional movement disorders during treatment. Mean follow-up differed between groups (ADSD: 10.0 vs. ADSD+LT: 7.22 vs. LT: 2.7 years; $p<0.001$). During follow-up, ADSD+LT patients had the highest incidence of new movement disorders. Essential tremor was the most common new diagnosis in all groups.

Multivariable Analysis

Table 4 summarizes the results of multivariable analyses of patient characteristics at presentation in models that compare ADSD+LT and LT to ADSD and in a model that compares LT to ADSD+LT. Except for LT vs. ADSD, where age showed a stronger association (OR per 1 year=1.14), age showed similar associations for ADSD+LT vs. ADSD

and for LT vs. ADSD+LT. In our patient population, the odds of having LT (OR=4.17) or ADLT+LT (OR=2.60) compared to ADSD were highest for women compared to men. There was no significant gender difference between patients with ADSD+LT and LT, although there was a suggestion for greater odds of LT vs. ADSD+LT among women than men (OR=1.53). The odds of having ADSD+LT (OR=4.24) or LT (OR=8.67) when compared to having ADSD alone also increased significantly with presence of a co-prevalent movement disorder diagnosis. Having a co-prevalent movement disorder was also associated with greater odds of LT compared to ADSD+LT (OR=1.86). Other hypothesized risk factors, including smoking history, alcohol use, and employment status did not attain statistical significance in multivariable logistic regression models. Inferences from multinomial logistic regression with generalized logits were similar to those from the standard dichotomous regression. For instance, the OR (95% CI) for LT compared to ADSD alone per 1-year increase in age at start of BTX was 1.14 (1.10–1.18) while it was 1.14 (1.10–1.19) when standard dichotomous regression was used.

DISCUSSION

This study compared patient characteristics of those diagnosed with ADSD, ADSD +LT, and LT in an attempt to gain better understanding of the epidemiology of and a window into the pathophysiology of these laryngeal movement disorders. Consistent with prior case series, ADSD affected the majority of our patient population (72.9%, n=475) and 20.6% (n=98) of those patients had concomitant laryngeal tremor.^{6,12} Coexistence of ADSD and tremor is perhaps not surprising since the same intrinsic adductory laryngeal muscles are overactive in both conditions.

Defining Spasmodic Dysphonia with Tremor

It has been acknowledged that epidemiologic, clinical features, and pathophysiologic mechanisms of patients with coincident tremor and dystonia, not specific to the larynx, remain unclear.¹⁸ This, in part, stems from controversy regarding the nature of tremor observed with dystonias such as ADSD.^{17–20} Tremor occurring without dystonia is commonly diagnosed as essential tremor - a symmetric, postural tremor occurring with regular frequency.^{17,18,20} As such, some describe isolated tremor of the vocal cords on phonation (e.g., LT) as essential voice tremor.^{17,25,26} According to the Movement Disorder Society (MDS) Consensus Statement, tremor of a muscle group affected by dystonia is defined as dystonic tremor.^{20,34} By this definition, ADSD + LT could be considered to be dystonic tremor. The characteristics of dystonic tremor can resemble the features of essential tremor (e.g., both are action tremors) making differentiation difficult. It is therefore imperative to understand what clinical features (if any) are unique to these disorders. Importantly, we avoid the use of dystonic tremor herein given existing controversy over nomenclature.

Age and Gender Differences

We identified several distinctive features between groups. First, age at presentation differed. Specifically, patients with LT presented at an older age than those with ADSD (69.3 vs. 52.5 years of age). This is concordant with prior studies, which found that ADSD and laryngeal

tremor patients presented between 39–56^{2,6,8,9,15,29–31} and 62–72^{24–26,32,35,36}, respectively. The size of the cohort uniquely allowed comparison between groups. We found ADSD + LT patients had an intermediate age at presentation in between that of ADSD (youngest) and LT (oldest). The only prior comparative study (n=150) similarly found that patients with both ADSD and laryngeal tremor were significantly older than those with ADSD alone (64.1 vs. 59.7 years).³

Just as seen for age, ADSD + LT had an intermediate prevalence of women (86.7%) compared to ADSD (74%) and LT (91.5%). Our findings are similar to those from case series, which found females make up 83–93% and 62–79% of patients with vocal tremor^{24–26,32,35,36} and ADSD^{2,6,8,9,15,29–31}, respectively. However, results herein also show a significantly greater proportion of women among those with ADSD + LT than among those presenting with ADSD.^{3,21}

The observed differences in age and gender provide clues into pathophysiology of these conditions. For instance, the general female predominance in these laryngeal movement disorders and the differential gender distribution among them may relate to hormonal influences on neural signaling and plasticity. In particular, estrogen has been shown to have both neuro-trophic and neuroleptic-like effects and can therefore modulate the dopaminergic system.³⁷ Age discrepancies between these diseases at treatment initiation may reflect inherent differences in pathophysiology, progression, or simply a difference in choice to present for treatment. In other words, if patients with vocal tremor had more gradual and less severe symptomology, they may present in a more delayed fashion. Mean diagnostic delays up to 6 years for patients with SD have been reported, suggesting a younger age of disease onset then reported herein.^{2,3,35,38} It is not clear how other considered movement disorders compare in this regard.

In patients with essential tremor, imaging and neuropathological evidence suggests that the cerebellum is a primary site of dysfunction.³⁹ Alternatively, patients with dystonia are thought to have dysfunctional homeostatic regulation of neural plasticity within the basal ganglia–cortical network.⁴⁰ Two postmortem and imaging studies on ADSD have also suggested that there are multiple sites of efferent and afferent motor system changes in patients with ADSD relative to healthy controls.^{41,42} Many of these changes are seen within the corticobulbar/corticospinal tract and its main input/output structures. However, some changes are also seen within the cerebellum or cerebellar circuits (i.e. inferior olive). Animal models have also found that cerebellar interactions with other neural circuits contribute to dystonia, but the nature of this interaction has not been elucidated.⁴⁰ Interestingly, neural abnormalities in ADSD and those with ADSD with laryngeal tremor have been shown to involve similar regions in sensorimotor processing and execution of motor commands.²¹ However, patients with concomitant tremor have additional cerebellar changes suggesting possible overlap with isolated laryngeal tremor of the voice. However, despite the intermediate gender and age distributions in this group, it remains unclear if this is a distinct disease or an intermediate presentation on a spectrum of laryngeal disorders including ADSD and isolated laryngeal tremor.

Perceived Inciting Events

The relationship between ADSD and psychiatric disease has long been debated. There is now compelling evidence that ADSD and tremor have identifiable neurological causes; nonetheless, the link between laryngeal movement disorders and psychological distress remains an area of active research. One reason for this continued interest is most patients with psychogenic voice disorders report rapid onset of symptoms after an illness or stressor.¹¹ In our cohort, 25% of patients reported a potential inciting event. The most common self-reported events related to psychologic stress or upper respiratory infections. Importantly, patients with ADSD did not report a significantly different rate of inciting events compared to those with tremor. These findings support the notion that SD is neurologic rather than psychogenic disease process, which may be precipitated by emotional or physical stress.^{3,10,30}

Family History

Family history of spasmodic dysphonia was rare in all groups (1.2%-2.6%), which is comparable to other studies (0–16%)^{6,8,29,30}, but is higher than the prevalence in the general population. Family history of tremor was more common in patients with a tremor component compared to ADSD. The higher prevalence in tremor patients is consistent with data from one small case series (n=34) in which 38% of patients had family history of tremor.²⁵ Our findings suggest that while sporadic cases of laryngeal movement disorders are more common than familial cases, tremor conditions may have a stronger underlying genetic predisposition.

Co-Prevalent Movement Disorders

Previous studies have shown 5–20%^{6,15,29} and 32.3–93%^{25,36} prevalence of co-prevalent movement disorders at presentation in patients with ADSD and vocal tremor. In the present study, patients with ADSD were found to have significantly fewer concomitant movement disorders (11.5%) compared to patients with ADSD + LT (38.7%) or LT (57.1%). As seen for age and gender distributions, patients with ADSD + LT had an intermediate co-prevalence between isolated ADSD and LT. In each group, non-laryngeal essential tremor was the most common concomitant diagnosis likely secondary to its greater prevalence in the general population.⁴³ Our findings are consistent with a prior study that has shown patients with ADSD with regular voice breaks having a lower rate of extralaryngeal tremor compared to those with laryngeal tremor.¹⁰

Development of New Neurological/Movement Disorder

At diagnosis, patients often ask whether they will develop additional movement disorders. Compared to ADSD, we found that patients with a tremor component were more likely to develop a secondary non-laryngeal movement diagnosis after initial presentation (ADSD: 0.8%, ADSD+LT: 7.5%, LT: 2.8%). Importantly, the likelihood of developing additional diagnoses depends on duration of follow-up. Thus, while only 2.8% of isolated tremor patients developed a new condition, mean follow-up duration was shortest in this group. Less duration of follow-up is owing to the relatively recent application of BTX to patients

with laryngeal tremors. With more extended follow-up this group may demonstrate an incidence rate comparable to or higher than ADSD + LT.

Comparing Laryngeal vs. Non-Laryngeal Movement Disorders

Patient characteristics in laryngeal movement disorders are somewhat different from those diagnosed with non-laryngeal dystonias and tremors, suggesting potential differentiating pathophysiological considerations. While essential tremor of the limbs has similar prevalence in males and females, there is a clear female predominance in patients with head tremors^{44,45} and craniocervical dystonias (e.g., blepharospasm).⁴⁶⁻⁴⁸ It is also interesting that patients with non-laryngeal essential tremor have a roughly 50% positive family history, which is substantially greater than that observed for laryngeal tremor.⁴⁴ A recent study has also found that somatosensory temporal discrimination processing is normal in essential tremor involving the upper limbs but altered in voice tremor.⁴⁹ Therefore, while isolated vocal tremors are typically referred to as essential vocal tremors, these must be distinguished from essential tremor of the limbs. Accordingly, the Tremor Investigation Group and MDS consensus criteria for essential tremor specifically exclude isolated vocal tremor.³⁴ Extrapolation of disease characteristics from non-laryngeal movement disorders to understand laryngeal disorders must therefore be done with caution.

Limitations

Retrospective cross-sectional data have inherent limitations. Errors in manual data extraction from medical records are possible. However, extraction was performed by an investigator and confirmed by a second independent investigator to optimize accuracy and integrity of data. Study design also precluded assessment of temporality between risk factors and dependent variables. Cross-sectional studies can only comment on associations and cannot directly infer causality. Although evaluation of rare diseases is difficult and our sample size is relatively small, this is among the largest cohorts of patients with spasmodic dysphonia and is the largest cohort with vocal tremor reported in literature.

CONCLUSION

Patients with co-prevalent ADSD and tremor demonstrate intermediate gender and age distributions between those with ADSD only and laryngeal tremor only. Family history of tremor and prevalent movement disorders are more similar between patients with laryngeal tremor (i.e. ADSD + LT and LT) than ADSD. It remains unclear if coprevalent ADSD and LT are distinct disease from ADSD and LT alone or whether it represents a different phenotype on a spectrum of laryngeal movement disorders.

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Figure 1. Study Flow Diagram with Inclusions and Exclusions

ADSD: Adductor Spasmodic Dysphonia, ABSD: Abductor Spasmodic Dysphonia, Mixed SD: ADSD + ABSD, Mixed Laryngeal Tremors: Combination of Lateral + Vertical and/or Antero-posterior Tremor

Table 1

Definitions of Laryngeal Tremor Directionality

Type of Tremor	Features on Flexible Laryngoscopy Exam ^a
Lateral	Repetitive rhythmic or non-rhythmic medial compression of the true and/or false vocal folds during phonation
Vertical	Global, rhythmic superior-inferior laryngeal movement
Antero-Posterior	Can be characterized in multiple ways: • Repetitive rhythmic or non-rhythmic anterior posterior compression of the true and/or false vocal folds during phonation • Repetitive rhythmic or non-rhythmic compression of medialized arytenoids towards the epiglottic petiole with or without compression of false vocal folds during phonation • Global laryngeal anterior-posterior repetitive movement without any compression within the laryngeal vestibule during phonation
Mixed	Repetitive rhythmic or non-rhythmic movement in any combination described above during phonation

^aFrequent aperiodicity of vocal fold vibration makes strobe light less useful; Movement of laryngeal structures is better appreciated under still light

Table 2

Univariate Comparison of Characteristics Among Patients with Adductor Spasmodic Dysphonia (ADSD), Laryngeal Tremor (LT), and ADSD with LT (ADSD+LT)

Variable	ADSD (n=377)	ADSD + LT (n=98)	LT (n=177)	P
Age at presentation, y	52.5 ± 13.4	63.9 ± 11.3	69.3 ± 10.5	<0.001
Gender, % women	74	86.7	91.5	<0.001
Race, %				0.33
White	80.1	81.6	84.8	
Black	4	5.1	5.7	
Other	15.9	13.3	9.6	
Smoking, %				<0.001
Never	67.4	73.3	71.4	
Past	16.9	23.3	23.8	
Current	15.6	3.5	4.8	
Alcohol, % current drinker	44.8	41.9	32.7	0.04
Employment, %				<0.0001
Employed	66.4	40.4	34.5	
Unemployed/student	10.3	9.6	7.6	
Retired	23.4	50	57.9	
Potential inciting event, %				0.29
No inciting event	73.8	70.4	78.7	
Upper resp. tract infection	9.7	9.9	3.9	
Psychological trauma ^a	4	3.7	5.2	
Physical Injury ^b	2.7	7.4	3.9	
Other ^c	9.7	8.6	8.4	
History of depression or anxiety, %	16.7	24.5	23.2	0.09
Family history of SD, %	2.6	2.4	1.2	0.6
Family history of vocal tremors, %	0.3	7.2	11.7	<0.001
Movement disorder at presentation, %	11.5	38.7	57.1	<0.001
Development of new movement disorder after initial presentation, %	0.8	7.5	2.8	0.001
Mean duration of follow-up, y	10.0 ± 7.6	7.22 ± 6.1	2.7 ± 6.3	<0.001

Values shown are means ± SD or %. P-values 0.004, the Bonferroni corrected P-value (0.05/13) are considered statistically significant.

Table 3

Co-Prevalent Non-Laryngeal Movement Disorders at Presentation

Variable, n (%)	ADSD (n=41)	ADSD+LT (n=36)	LT (n=100)
Essential Tremor	20 (49)	27 (75)	88 (88)
Other Airway Tremor ^a	2 (5)	3 (8)	6 (6)
Head and Neck Dystonia ^b	10 (24)	3 (8)	3 (3)
Limb Dystonia	4 (10)	2 (6)	0 (0)
Other ^c	5 (12)	1 (3)	3 (3)

^aPalatal or pharyngeal Tremor,^bBlepharospasm, Oromandibular Dystonia, Torticollis,^cAlzheimers Disease, Parkinsons Disease, Restless Leg Syndrome, Multiple Sclerosis

Table 4

Multivariable Logistic Regression Analyses Evaluating Comparison between Adductor Spasmodic Dysphonia (ADSD), Laryngeal Tremor (LT), and ADSD with LT (ADSD+LT)

Variable	Odds ratios (95% Confidence Intervals) ^a		
	ADSD+LT vs. ADSD	LT vs. ADSD	LT vs. ADSD+LT
Age at presentation (per 1 year increase)	1.07 (1.03–1.11)	1.14 (1.10–1.19)	1.07 (1.03–1.11)
Gender (Women vs. Men)	2.60 (1.03–6.53)	4.17 (1.64–10.6)	1.53 (0.50–4.65)
Race			
Black vs. white	3.70 (0.88–15.6)	4.10 (0.84–20.0)	1.40 (0.36–5.39)
Other race vs. white	0.73 (0.26–2.06)	1.05 (0.43–2.55)	1.61 (0.52–4.94)
Smoking			
Current vs. Never	0.34 (0.08–1.42)	1.57 (0.74–3.32)	2.02 (0.46–9.02)
Past vs. Never	1.33 (0.60–2.92)	0.35 (0.10–1.23)	1.19 (0.54–2.62)
Alcohol (Current vs. Never)	0.93 (0.47–1.82)	1.31 (0.68–2.51)	1.078 (0.53–2.18)
Employment			
Retired vs. Employed	0.75 (0.30–1.87)	0.49 (0.21–1.14)	0.63 (0.27–1.50)
Unemployed/student vs. employed	0.76 (0.24–2.46)	0.44 (0.13–1.49)	0.57 (0.17–1.89)
Potential Inciting Event (Yes vs. No)	0.70 (0.34–1.45)	0.60 (0.30–1.21)	0.63 (0.30–1.31)
Anxiety/Depression (Yes vs. No)	1.69 (0.81–3.51)	1.68 (0.79–3.58)	0.79 (0.39–1.61)
Co-Prevalent Movement Disorder (Yes vs. No)	4.24 (2.01–8.96)	8.67 (4.39–17.1)	1.86 (0.99–3.50)

^aFor each dependent variable, all potential risk factors were modeled simultaneously in a logistic regression model and are adjusted for each other. Inferences from multinomial logistic regression with generalized logits were similar to those from standard dichotomous logistic regression.